UNIVERSITY OF BUEA

FACULTY OF SCIENCE

DEPARTMENT OF MICROBIOLOGY AND PARASITOLOGY

EFFECTS OF MORBIDITY MANAGEMENT ON DISABILITY AND DEPRESSIVE SYMPTOMS OF PODOCONIOSIS PATIENTS, 12 AND 24 MONTHS FOLLOWING INTERVENTION IN THE NORTH WEST REGION OF CAMEROON

A dissertation submitted to the Department of Microbiology and Parasitology, Faculty of Science, University of Buea, in partial fulfilment of the requirements for the award of Master of Science (M.Sc.) Degree in Epidemiology and Control of Infectious Diseases

By

NDEUGUE NOUYOU MICHEL

(SC19P180)

B.Sc. Clinical Biochemistry

Supervisor**:** Dr. ESUM MATHIAS EYONG Co-Supervisor: Dr. NJOUENDOU ABDEL JELIL

October, 2022

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DEDICATION

To everyone reading this dissertation to make the world a better place

CERTIFICATION

This is to certify that the research work entitled 'Effects of Morbidity Management on Disability and Depressive symptoms of Podoconiosis patients, 12 and 24 months following intervention in the North West Region of Cameroon' was carried out by **NDEUGUE NOUYOU MICHEL (SC19P180)** in the Department of Microbiology and Parasitology in partial fulfilment of the requirements for the award of Masters of Science (M.Sc.) degree in Epidemiology and Control of Infectious Diseases under the supervision of :

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ABSTRACT

Podoconiosis is a non-communicable, non-filarial elephantiasis originating from long-term exposure of bare feet to irritant red clay soil. It is known to have affected approximately 4 million people globally. Deformities of the lower legs often result to chronic disability, depression and psychosocial consequences, which all together negatively correlates with Quality of Life. Worldwide, there is limited knowledge on the effects of morbidity management on disability and depressive symptoms related to podoconiosis. In Cameroon, no such study has been done. The aim of this study was to evaluate the effects of morbidity management on the disability and depressive symptoms related to podoconiosis over 24 months in the North West Region. The study design used was a prospective design. Data was collected using the disability assessment schedule and patient health questionnaire. A total of 199 participants were recruited and 161 (80.9 %) followed measure sequence without discontinuing. The median disability score at baseline was 31.3. This decreased significantly to 8.4 and 14.6 at 12 and 24-month ($p<0.001$) respectively. Of the 161 participants, 65 % had at least mild depression at baseline this dropped significantly ($p<0.001$) to 31 % at 24-month. There was no significant association between good compliance and decreased disability ($p = 0.408$) estimate = -2.89, 95% CI: -7.37, 1.58. Participants with good compliance to lymphoedema management had an overall mean depressive symptoms scores of 1.57 points significantly lower ($p = 0.008$) than those who poorly complied (95% CI: -2.19, -0.19) after adjusting for age and educational duration. Participants gained an average of 1.3workdays/month and if extrapolated to the estimated 41556 cases in Cameroon, this translates into 3553 person-years of productive time gained over the 24 months period as a result of decreased disability. Morbidity management

significantly decreases disability and depressive symptoms related to podoconiosis in the North West Region on Cameroon.

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LIST OF ABBREVIATIONS

ADLA	Acute Dermatolymphagioadenitis
DLQI	Dermatology Life Quality Index
Dom	Domain
HRQoL	Health Related Quality of Life
ICF	International Classification of Functioning, Disability and Health
NTD	Neglected Tropical Disease
PHQ	Patient Health Questionnaire
QoL	Quality of Life
WHO	World Health Organisation
WHODAS	World Health Organisation Disability Assessment Schedule
C.I	Confidence Interval
OR	Odds ratio
EMM	Estimated Marginal Mean
LM	Lymphoedema management

DEFINITION OF TERMS

Activity limitation is the difficulty encountered by an individual in executing a task or action.

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest which can interfere with an individual's daily functioning.

Disability or functional limitations is the inability to adequately or independently perform routine daily activities such as walking, bathing and toileting; the negative aspects of the interaction between a person with a health condition and his or her context (environmental or personal factors).

Disease burden is the impact of a health problem on a given area, and can be measured using a variety of indicators such as mortality, morbidity or financial cost.

Lymphoedema management is a combination of regular limb washing, exercises, elevation, proper footwear and bandaging (for cases with wounds).

Morbidity management: Embodies lymphoedema management practices and other therapies to treat co-occurrence and reduce or prevent inflammatory episodes linked to podoconiosis.

Participation restriction is a problem experienced by an individual in involvement in life situations.

Quality of life (QoL): The World Health Organisation defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".

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CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Podoconiosis is a neglected tropical disease lymphoedema common amongst subsistence farmers in tropical areas, who have had prolong exposure to irritant red clay soil of volcanic origin on a background of genetic susceptibility. It is clinically distinguished from lymphatic filariasis (LF) through it being ascending, usually bilateral but asymmetrical and almost always limited to below the knees (Deribe *et al*., 2016; WHO, 2018). It seems not to be directly caused by any bacteria, parasite or virus but rather an unusual inflammatory reaction geochemical disease common among bare foot subsistence farmers who are in long-term contact with irritant red soil of volcanic origin (Price, 1981; Davey *et al*., 2009).

Neglected tropical diseases (NTDs) are a group of primarily infectious diseases that also include some exposure-related conditions such as snake-bite and podoconiosis affecting approximately 1 billion sufferers globally. Hamill and colleagues stated that people are neglected, not diseases; and further highlighted the relationship between disability and neglected tropical diseases. WHO has not officially declared podoconiosis as an NTD. However, its elimination and control is integrated into the lymphatic filariasis morbidity management and disability prevention program in countries such as Ethiopia and Rwanda (Hamill *et al*., 2019; Wanji *et al*., 2021; WHO, 2021).

One of the risk factors of podoconiosis is environmental conditions of high altitude above 1000m and high annual rainfall greater than 1000mm. Various studies have showed a higher prevalence among active group of people (especially uneducated subsistence farmers) who find it difficult to read or write (Bekele *et al*., 2016; Wanji *et al*., 2021).

NTDs affect about one billion people globally, and podoconiosis being one of the NTDs causes chronic disability (which could be psychological, mental and much more physical) and morbidity rather than death (Davey and Newport, 2010; Mousley *et al*., 2015). Evidence is emerging that shows increased mental distress and disorder amongst people with several neglected tropical diseases (NTDs). Podoconiosis just like most NTDs imposes huge burdens on affected individuals, their families and communities, not only in terms of physical disability, but also in terms of mental distress, depression, stigma and loss of economic productivity (Bekri *et al*., 1998).

The health related quality of life (HRQoL) assesses how the participant's well-being may be affected over time by a disease such as podoconiosis and its debilitating effects. The instrument has become an important component of public health surveillance and comprises valid indicators of unmet needs and intervention outcome. Measures on HRQoL make it possible to demonstrate scientifically the impact of health on quality of life (QoL) going beyond the old paradigm that was limited to what can be seen under the microscope or other biomedical instruments hence bridging the boundaries between social, mental and medical disciplines (Dominick *et al*., 2002). Thirteen studies were found in a literature search that assessed quality of life of patients with NTDs using standardised scales. One of these looked at dermatological quality of life in podoconiosis, and found a significant reduction in quality of life comparable to other dermatological conditions (Legesse, 2008).

Cameroon is thought to be among the countries with the highest burden of podoconiosis (Wanji *et al*., 2008). Lymphoedema caused by LF or podoconiosis has been shown to be debilitating, demobilising and stigmatising, giving rise to social isolation, loss of income, depression, emotional and mental distress, (Perera *et al*., 2007; Obindo *et al*., 2017). Due

to lack of understanding of the geographical distribution of the disease, intervention against the disease is minimal (Wanji *et al*., 2018).

The major concern regarding the effectiveness of morbidity management is whether it can improve podoconiosis participants' clinical outcomes (decrease frequency of inflammatory episodes and reverse swelling to lower stages) and hence have a positive effect on their disabilities and symptoms of depression. Lembcke back in 1952 stated that it is not how well or how frequent a medical service is given, but how closely the result approaches the fundamental objective of prolonging life, relieving distress, restoring function and preventing disability (Lembcke, 1952). It is in this light that this study was designed to evaluate the effectiveness of the intervention (morbidity management) on the disability and depressive symptoms related to podoconiosis by monitoring changes in scores over time (24 months follow up).

1.2 Statement of the problem

An estimated 41556 individuals live with podoconiosis in Cameroon and about 5.2 million people are living in high endemic areas. The burden of the disease ranges from low to severe disability affecting the quality of life of its patients hence, resulting in low productivity, and major economic and social consequences (Davey *et al*., 2009; Deribe *et al*., 2018a). Patients suffering from podoconiosis often have a primary notion that it was been inflicted on them by an opponent, and more to that, some communities accuse individuals for being the cause of their problems. These and other stigmatising factors could have led to dead due to severe depression or emotional torture since some patients consider not being part of the world and feel like giving up.

A good number of studies have been carried out linking physical, social, and mental health with podoconiosis. Some of these studies assessed depression (Semrau and

colleagues), disability, and QoL (Mousley and colleagues) in podoconiosis patients but little research has focused on the assessment of the lasting effects of morbidity management on the disability and depressive symptoms of podoconiosis patients, which this study sets out to investigate (Mousley *et al*., 2015; Semrau *et al*., 2020).

1.3 Rationale of the study

Disability and depression have always been associated with NTDs. In our study, podoconiosis known in the past years to be a neglected of the NTDs had enormous impact on patient health (and mental health) ranging from social isolation, low self-esteemed, enacted stigma to suicide ideation and other major depressive disorder (Ayode *et al*., 2016). The lag in knowledge on podoconiosis treatment (morbidity management) has brought about considerable pain in the process of seeking a treatment for the disease by podoconiosis patients and their family members.

Morbidity management can reduce disability as such increases interpersonal interaction, participation in community activities, self-care, learning abilities, and reduce days of work lost. The intervention can also decrease depression severity and prevent depressive disorders hence having a positive impact on patients' mental health specifically and Quality of life related to podoconiosis. A successful improvement due to morbidity management, if there be, could further demystify misconceptions about the aetiology and prevention of podoconiosis. These misconceptions have been shown to be the root cause of disability aggravation, depression severity and social stigmatisation in podoconiosis patients as stated by Yakob and colleagues (Yakob *et al*., 2008).

In Cameroon, there exists only one morbidity management centre for podoconiosis which is also a clinical trial centre located in Nkwen, Bamenda. The intervention could be of economic benefits in terms of considerable work days saved and because of this, policy

makers could be inform on the importance of creating more morbidity management centres and lay emphasis on the need to prioritise morbidity management and prevention programmes (MMPP) nationwide.

Based on the disease burden, misconceptions and high podoconiosis endemicity in some regions of Cameroon and in the North West Region specifically, it is therefore important to assess the effects of morbidity management on the patients' disability, depressive symptoms and inferentially the quality of life which could bring a turn-around in their social life and economic development. This could increase national productivity (as the incapacitated days or days in which patients were unable to work probably decreases due to the intervention) especially in agricultural products since most patients are subsistence farmers and business men and women (Table 3) as started by Negussie and colleagues (Negussie *et al*., 2018).

1.4 Hypothesis

We hypothesised that:

- Morbidity management decreases disability and depressive symptoms in podoconiosis participants.

1.5 Research Questions

1. What effect does morbidity management have on disability (functioning outcomes) of podoconiosis patients at 12-month (midline) and 24-month (endpoint) follow up?
2. What is the effect of morbidity management on the depressive symptoms over a period of 12 and 24 months following treatment onset?
3. What is the additional benefit of good compliance over poor compliance to lymphoedema management on study outcomes following measure sequence?

1.6 Objectives

1.6.1 Main Objective

The main objective of this study was to evaluate the effect of morbidity management on functioning outcomes and depressive symptoms in podoconiosis patients, in the North West Region of Cameroon.

1.6.2 Specific Objectives

The specific objectives were to:

1. Assess the effect of morbidity management on the disability of podoconiosis patients, 12 and 24 months following intervention;
2. Assess the effect of morbidity management on depressive symptoms over a period of 12- and 24-months following intervention;
3. Estimate the additional benefits of good compliance to lymphoedema management over poor compliance on disability and depressive symptoms over time.

CHAPTER TWO

LITERATURE REVIEW

2.1 Historical overview of the theory and research literature

2.1.1 Epidemiology of Podoconiosis

The distribution of podoconiosis shows a correlation with the distribution of red clay soil derived from volcanic rock probable reason why it is common in highland areas of Africa, India, and Central America (Davey *et al*., 2007a). The global epidemiology of podoconiosis is largely uncertain irrespective of its interest worldwide. This is partly due to the absence of accurate and easy-to-use diagnostic tools such as a point-of-care diagnostic test. Understanding the number of cases suffering from podoconiosis, the disease geographical distribution, and population at risk are of great importance in estimating the burden of the disease in endemic countries (Deribe *et al*., 2017a; Wanji *et al*., 2018). Podoconiosis is endemic in 32 countries and current global estimates suggest that there are approximately 4 million cases in Africa, parts of Latin America and South East Asia (Tekola *et al*., 2012). It is second only to bancroftian filariasis as the leading cause of lymphoedema in tropical countries (Davey *et al*., 2007a; Molyneux, 2012). A recent review has summarised the global distribution of podoconiosis as shown in figure 1A and 1B (Deribe *et al*., 2018b).

Although high prevalence of podoconiosis has been reported intermittently across a range of settings, it has neither been prioritised to an extent in interventional studies nor in research programmes. This may be due to the lack of resources for new health initiatives, which is a common problem in the low-income tropical countries where this disease is present. In Africa, only two countries (Ethiopia and Rwanda) are known to have been

reporting podoconiosis within their routine health management information systems (Deribe *et al*., 2017b).

2.1.1.1 Countries most affected by Podoconiosis

People most affected by podoconiosis mainly live in tropical countries of Africa, Central and South America, and South-East Asia (figure 1A and 1B). In Latin America countries like; Brazil, Colombia, Costa Rica, Ecuador, El Salvador, French Guiana, Guatemala, Honduras, Mexico, Peru and Suriname, were affected. Likewise in Asia, cases have been found in India, Sri Lanka and Indonesia. Affected countries in Africa are; Angola, Burundi, Cameroon, Cape Verde, Chad, Democratic Republic of Congo, Equatorial Guinea, Ethiopia, Kenya, Madagascar, Mozambique, Niger, Nigeria, Rwanda, São Tomé and Príncipe, Sudan, Tanzania and Uganda (Deribe *et al*., 2018b; Wanji *et al*., 2021). Mapping studies further suggest a global prevalence ranging from 0.10 to 8.08% that is specifically high in the tropical zones of Africa with the three highest prevalence rates in Uganda (4.5%; Eastern regions), Ethiopia (7.4%, South-western and Central regions), and Cameroon (0.5 - 8.1%; highlands of North-Western regions), (Wanji *et al*., 2008; Nenoff *et al*., 2010; Geshere *et al*., 2012; Deribe *et al*., 2013; Deribe *et al*., 2017b; Deribe *et al*., 2018a Deribe *et al*., 2018b; Deribe *et al*., 2019;). In contrast, Rwanda have a relatively low prevalence but podoconiosis is widely distributed throughout the country (Deribe *et al*., 2019), highlighting that this neglected tropical disease is a serious health problem in Africa (Deribe *et al*., 2020).

2.1.1.2 Podoconiosis in Cameroon

In a study carried out to map the geographical distribution of podoconiosis in Cameroon using parasitological, serological, and clinical evidence to exclude other causes of lymphoedema, it was demonstrated by Deribe and colleagues that Cameroon had a low

prevalence but an almost nationwide distribution of cases as shown in figure 1C. The overall prevalence of podoconiosis was 0.5% with at least one case in all regions of Cameroon, except Adamawa (where no case was identified in the two villages surveyed). The highest prevalence rates were found in the North West (1.7%) and North (1.0%) regions of the nation. The majority of affected individuals were in the age group of 25-64 years. Deribe and colleagues also reported that national population living in areas environmentally favourable to podoconiosis was estimated to be 5.2 million, which corresponds to 22.3% of Cameroon's population in 2015. Countrywide, in 2015, the number of adults estimated to be suffering from podoconiosis was 41556. Four regions (Centre, Littoral, North and North West) contributed to 61.2% of the cases (Deribe *et al*., 2018a). The disability and deformity caused by podoconiosis in patients have been shown to have serious economic and social consequences (Mousley *et al.*, 2013).

Studies on the spatial distribution of podoconiosis cases who had lived for more than 10 years in the North West Region of Cameroon revealed that 48.70% of registered individuals were adults. A total of 2143 lymphoedema cases were identified by community health investigators, giving a prevalence of lymphoedema of 1.0%. The prevalence of podoconiosis in the study area was 0.48% (Wanji *et al*., 2018).

2.1.1.3 Podoconiosis in the North West Region Cameroon

Podoconiosis had previously been demonstrated in some of the health districts, where out of the 817 subjects clinically examined, 484 came from Ndop health district (61.8% females) of which 66 cases were confirmed, and 333 (with 57% male) from Tubah whereby 49 cases were confirmed indicating the presence of elephantiasis of non-filarial origin (Wanji *et al*., 2008). In a cross-sectional study carried out in 19 district hospitals in the North West region, lymphoedema cases in early stages were more frequent than

chronic stages. Of the 2143 lymphoedema cases, the highest proportion was recorded for stage 2 (60.6%), followed by stage 3 (25.7%) and stage 4 (11.5%). Stage 5 was the least common (2.2%). All lymphoedema stages appeared to increase with age. Stages 2 and 5 were more prevalent in patients over 50 years old (Wanji *et al*., 2018).

The prevalence varied between health districts from 0.16% in Oku to 1.92% in Bafut. The disease was more prevalent in Bafut (1.92%), Batibo (1.64%) and Njikwa (1.14%). Women noticed swellings earlier than men. The overall prevalence was estimated to be 0.49%, ranging from 0.16 to 1.92% by Health District. Sex and age were identified to be risk factors for podoconiosis. The mean prevalence was far lower than that (8.1%) reported from two health districts in this region (Wanji *et al*., 2008; Wanji *et al*., 2018).

Figure 1C shows the distribution of surveyed communities and background points for podoconiosis across Cameroon. “Presences” are points where podoconiosis was present. “Absences” are areas where the absence of podoconiosis has been confirmed. “Pseudo-absences” are points to compensate for the lack of absence data. A database of 748-located prevalence records of the disease was compiled and the prevalence data were assembled in two cross-sectional studies conducted in Cameroon (Deribe *et al*., 2018a).

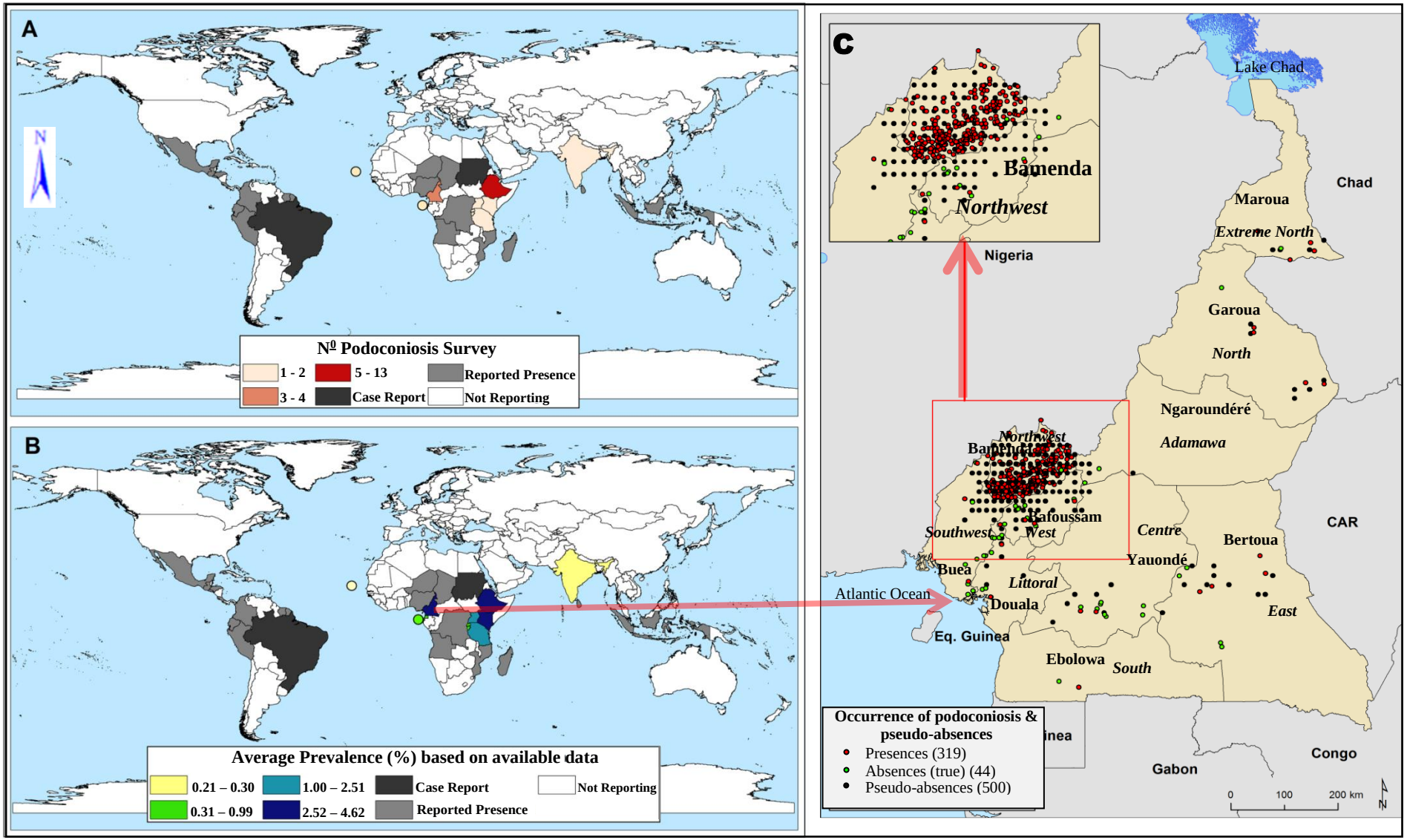


Figure 1: Geographical distribution of A) Surveys included, B) Prevalence of Podoconiosis. Dots represent various island nations. Adopted from: Deribe et al., 2018b; https://doi.org/10.1371/journal.pntd.0006324.g002) and C) Nationwide distribution of podoconiosis in Cameroon (Adapted from: Deribe *et al.*, 2018a).

2.1.2 The Pathogenesis of Podoconiosis

The aetiology of podoconiosis has not yet been completely understood. Based on existing evidence the most accepted cause of podoconiosis is inorganic particle-induced inflammatory response on a background of genetic susceptibility (Davey *et al*., 2007b). Mineral particles, absorbed through the skin of the foot, are taken up by macrophages in the lower limb lymphatic and induce an inflammatory response in the lymphatic vessels, leading to fibrosis and obstruction of the vessel lumen. This leads initially to edema of the foot and the lower leg, which progresses to elephantiasis: gross lymphoedema with mossy and nodular changes of the skin (Price, 1976). It has also been reported that the interactions between genetic and environmental factors triggered this inflammatory response that led to lymphoedema and fibrosis though the mechanism by which soil particles enter the feet through the skin still remain unclear (Tekola *et al*., 2012; Le Blond *et al*., 2017).

2.1.3 Genetics and podoconiosis

One of the striking features of podoconiosis is that a small proportion of individuals who are exposed to red clay develop the disease. Familial clustering of cases has been noted in affected communities in Ethiopia, Rwanda and Burundi (Price, 1972; Price, 1976). These studies demonstrated the genetic susceptibility of some families to the disease than others. Furthermore, heritability of podoconiosis was estimated to be 0.629 with a phenotypic variance of about 63% accounted for by genetic factors. In addition, Davey and colleagues suggested that for better understanding of the gene-environmental interaction further studies need to be carried out on the pathogenesis of podoconiosis and complex multifactorial conditions (Davey *et al*., 2007b).

2.1.4 Clinical features and diagnosis of podoconiosis

Early symptoms of podoconiosis include itching of the skin of the forefoot and recurrent episodes of burning (dysesthesia) and oedema of the foot or lower leg, especially after periods of intense physical activity. As lymphatic vessel obstruction progresses, established lymphoedema sets in and elephantiasis occurs. This can clinically vary from soft subdermal lymphoedema to hard or leathery leg elephantiasis, consisting of fibrosis of the skin and sub cutis, which end up thick remarkably. Over the years, the increase in the diameter of the leg persists and can progress to severe elephantiasis. The skin often shows hyperkeratosis, moss-like papilloma, and hard nodules. Local complications include wound infections and ulcerations. Diagnosis is based on location (usually in population living at high altitudes more than 1000 meters above sea level), history, clinical findings and absence of microfilaria or antigen on immunological card test (Price, 1976; WHO, 2018).

2.1.5 Stages of podoconiosis

There are five degrees of severity, depending on how far proximal the non-filarial elephantiasis has spread and the severity of skin nodules, bands and ridges. This staging system has proven to be reproducible and thus is a good basis for further epidemiological studies on podoconiosis (Nenoff *et al*., 2010). The initial draft of clinical staging system was based on the 7-stage Dreyer scale, namely, swelling reversible overnight; swelling that cannot be reversed overnight; shallow skin folds; knobs; deep skin folds; mossy lesions and social disability (Dreyer *et al*., 2002). The clinical staging system for podoconiosis was modified (to 5 numeric staging) from the Dreyer staging system for filarial lymphoedema after it became clear that the disease progression of filarial and podoconiosis lymphoedema were quite different. In addition to the 5 numeric staging stated in table 1 with their corresponding stage photographs in figure 2, the following

measurements were taken; the greatest below the knee circumference, and record of the presence (M+) or absence (M-) of mossy changes of both legs (Tekola *et al*., 2008).

Table 1: Stages of podoconiosis (Tekola *et al*., 2009)

Stage	Stage Headline	Description
1	Swelling Reversible overnight	The swelling is not present when the patient first gets up in the morning
2	Swelling Not completely reversible overnight.	Persistent swelling that does not reach above the knee. If the knobs or bumps are seen or felt, they are only present below the ankle.
3	Swelling Not completely reversible.	Persistence swelling that does not reach above the knee. Knobs or bumps can be seen or felt above the ankle as well as below.
4	Swelling Not completely reversible.	Persistence swelling that is above the knee. Knobs or bumps can be seen or felt at any place on foot or leg.
5	Joint fixation	The ankle or toe joints become fixed and difficult to flex or dorsiflex. This may be accompanied by apparent shortening of the toes.

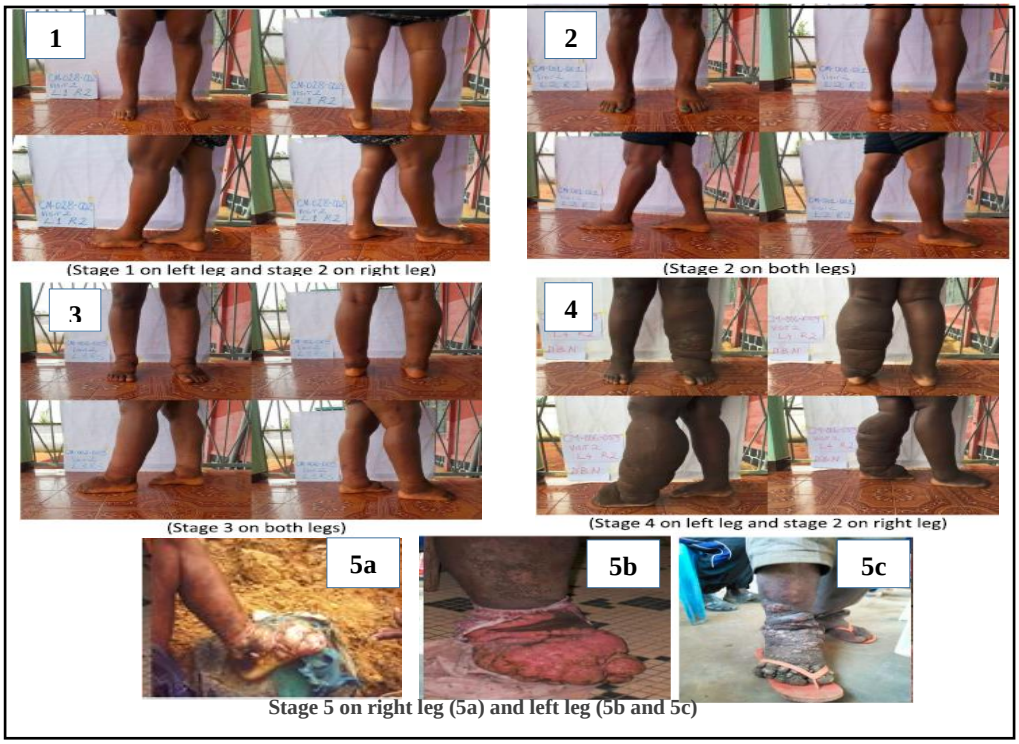


Figure 2: Stages described on table 1(stage 5 and a four sided view of stage 1 to 4)

Source (adapted): Wanji *et al*., 2021

2.1.6 Prevention, management and treatment of podoconiosis

Prevention of podoconiosis is classified in three phases. The primary phase consists of avoiding skin contact with irritant soil by wearing sturdy shoes. The secondary prevention is geared towards preventing the progression of early clinical manifestation of the disease, education on foot hygiene where patients are taught on how to cater for their feet daily by using soap, water, antiseptics, emollients and wearing socks and shoes. Tertiary prevention includes management of advanced stages of lymphoedema (stages 4 and 5). Measures of secondary prevention are added to elevation of affected limb, and compression therapy. Compression bandages are effective for managing oozing feet. Prolong feet elevation for hours have been shown to be effective but it is not practical. Severe hyperplasia (tissue enlargement) and nodules can be surgically treated. Long term results using Charles's surgery method which involved removal of skin, subcutaneous tissues and closing the defect with skin graft were disappointing (Nenoff *et al*., 2010).

Podoconiosis has a curable pre-elephantiasis phase. However, once elephantiasis is established, podoconiosis persists and can only be managed to halt progression to a more advanced stage (Nenoff *et al*., 2010). Simple lymphoedema management consisting of foot hygiene, foot care, wound care, compression, daily exercises and elevation, treatment of acute attacks, use of shoes and socks to reduce further exposure to the irritant soil were recommended than Charles's surgical method (Price, 1990). Nevertheless, a recent study has shown that surgical nodulectomy (removal of nodules) is safe, provides an opportunity for patients to wear shoes again, helps to greatly reduce number of bacterial infections hence enhancing an additional benefit as patients can easily clean their affected leg(s), greatly decreases Acute Dermatolymphagioadenitis (ADLA) occurrence, and significantly improve the quality of life with no serious complications in podoconiosis patients with late stages (stage 4 and or 5) (Enbiale *et al*., 2021).

2.1.7 Socio-economic implications of podoconiosis

Due to the development of lymphoedema stigmatisation, and also based on the fact that several studies showed podoconiosis affected individuals are excluded from school, not allowed to attend churches or mosques or other public and social gatherings, many patients live a less productive and poor social life (Price, 1977; Deribe *et al*., 2015). Moreover, it was shown that healthy people do not want to marry affected persons or anyone from a podoconiosis affected family because patients (in higher stages) have physical limitations and thus it is believed that they cannot properly help in fulfilling their household responsibilities and cater for children (Ayode *et al*., 2016). To some extent, affected individuals are even discriminated or look down on by family members and it has been shown that approximately 13% of podoconiosis patients experienced stigmatisation in the society (schools, markets, job site, matrimonial homes just to cite a few) (Fuller, 2013; Ayode *et al*., 2016). About 55% of healthy individuals showed a stigmatising attitude towards individuals affected by podoconiosis (Tekola *et al*., 2009). In addition, patients also experienced stigmatisation in the healthcare system by professional staff and more than half of the respondents believed that podoconiosis was an infectious disease and were afraid of contracting it during patient care (Yakob *et al*., 2008; Yakob *et al*., 2010).

The main reason for social stigma is the missing education about the disease and misconceptions about prevention, cause, symptoms and treatment in endemic areas (Yakob *et al*., 2008; Tekola *et al*., 2009). Consequently, patients feel guilty, hide and isolate themselves from the rest of the community members; some even consider suicide or suffer from other depressive symptoms (Yakob *et al*., 2010; Ayode *et al*., 2016; Semrau *et al*., 2019).

In general, patients with podoconiosis have significantly lower quality of life (QoL) scores than control persons and more than half of the patients suffer from movement restrictions, especially during episodes of ADLA attack (Bartlett *et al*., 2016; Deribe *et al*., 2019). Thus, ordinary household activities can no longer be performed optimally and so patients have less energy resulting to less productiveness (Fuller, 2013). Following a study published by Alemu and colleagues, 97% of podoconiosis patients experienced an average of 5.5 ADLA episodes yearly whose occurrence was higher than that reported for bancroftian elephantiasis patients in other countries. Each ADLA attack took an average of 4.4 days, consequently a loss of approximately 24 working days was experienced annually and this has a negative impact on quality of life (Alemu *et al*., 2011).

Podoconiosis leads to progressive disability when left untreated, resulting to disfiguring condition which has significant social impact. Affected people often face forms of severe stigma such as isolation, exclusion from community event and barriers to employment, education, or marriage. This health related stigma can further lead to harmful delays in diagnosis or treatment seeking due to fear, shame, or lack of economic capital (Deribe *et al*., 2013).

The stigmatisation and social barriers lead to an economic burden for podoconiosis affected individuals likewise on a larger economic scale (Destas *et al*., 2003; Henok, 2008). It was estimated that the total economic burden of podoconiosis is US$213.2 million annually in Ethiopia, of which 91.1% was due to productivity costs, and the average economic burden per podoconiosis patient was US$136.90 (Deribe *et al*., 2020). In addition, it was also shown that the majority of affected individuals fall into the most economically productive age group and moreover a loss of roughly 45% of all working days was predicted (Henok, 2008; Tekola *et al*., 2012; Tembei *et al*., 2018; Deribe *et al*., 2020). In studies, around 44.9% of podoconiosis patients work only occasionally, 32.4%

avoid heavy physical work or work fewer hours (21.9%), 8% stopped working. More so, 78% stated that they were poorer than healthy neighbours and almost all patients (96.4%) noticed a decline in their income following the development of podoconiosis (Molla *et al*., 2012; Fuller, 2013). This was also confirmed by a study in Cameroon, where the average household income in podoconiosis-affected households was less than half of non-podoconiosis affected households. Moreover, podoconiosis households spend more than twice as much on treating diseases than normal households (Tembei *et al*., 2018).

In regard to disability-adjusted life years (DALYs), Deribe and colleagues stated 182 DALYs per 100,000 inhabitants and that the consequences of podoconiosis caused 24% of the total NTD DALYs and 0.5% of the total DALYs in Ethiopia. The consequences of podoconiosis are therefore not only severe for individuals, they also mean a considerable weakening of the economic performance of the entire country, highlighting the importance of interdisciplinary research about podoconiosis to obtain knowledge, especially about the origin, immunology and diagnosis of this very neglected tropical disease to implement prevention and control programmes (Deribe *et al*., 2020).

2.1.8 Psychological implications in podoconiosis patients

Mental health conditions (such as mental, neurological and substance use disorders, suicide risk, associated psychosocial, cognitive and intellectual disabilities) contribute substantially to the global burden of disease. NTDs in general and podoconiosis in particular being a neglected of NTDs have common determinants and risk factors which combine and increase negative health consequences in patients. Thus, the poorest, most marginalised people are at risk, are most likely to be affected by both conditions and are the least likely to have access to care. It is so closely associated with poverty that

reductions in their prevalence are recognised as markers for progress in economic development in the Sustainable Development Goals (SDGs) (Bartlett *et al*., 2016)

Depression is the most significant of mental health problems on a global scale, being the third leading cause of non-fatal disease burden worldwide and representing 4.3% of total disability-adjusted life years (DALYs) (Bartlett *et al.*, 2016). A research carried out in Rwanda demonstrated that among 1143 patients screened for podoconiosis after random selection in 80 sectors, up to 914 had podoconiosis and 68% of these patients were reported to have depressive symptoms (Semrau *et al*., 2020). A recent cross-sectional study in Cameroon found that 38.5% (over one-third of the participants) of people with podoconiosis or lymphoedema of another cause displayed at least mild depressive symptoms (Semrau *et al*., 2019).

2.2 The theory and research literature specific to the topic

Disability arises when someone with a health condition like podoconiosis experiences an impairment such as pain or slowness or reduced mobility that causes difficulties in performing activities (standing for some time or longer, walking a kilometre, getting dressed, bathing, concentrating, household responsibilities, visiting new places or learning new things) potentially resulting in participation restrictions such as inability to work or socialise in the community (Hamill *et al*., 2019). Molla and colleagues in their publication titled Patients' perceptions of podoconiosis causes, prevention and consequences in East and West Gojam, Northern Ethiopia, found that many podoconiosis patients (about 60%) reported physical impairment (movement) due to the disease and about 27% said their movement was impaired by ADLA attack episodes. To mitigate this physical impairment, patients adopted some coping strategies such as; working only

occasionally, avoiding physically demanding tasks, working fewer hours or completely stopping work (Molla *et al*., 2012).

Mental distress has also been found to be significantly higher among people with podoconiosis in Ethiopia compared with healthy controls (Mousley *et al*., 2015). However, the pathway from this health condition is not the same for everyone. It is buffered by personal factors such as; wealth, social support, education and environmental factors, including the existence of legislation protecting rights or the availability of assistive devices (Kuper, 2019; Fischer *et al*, 2019).

Depression is of great significance to these patients because in addition to personal suffering, it has been associated with poor QoL, greater disability, faster progression physical symptoms, greater decline in cognitive skill and ability to care for oneself, poorer treatment compliance and greater caregiver distress (Menza *et al.,* 2009). In fact depression seems to be more predictive of QoL than motor disability in diseases like Parkinson's disease (Diego *et al*., 2021). Moreover, the physical health domain of QoL had been shown to reduce by 1.92 units among patients with depression who live alone as compare to those living with their own families (Shumye *et al.*, 2019).

Lymphoedema, deformities, and painful inflammatory episodes are both common to podoconiosis and LF sufferers. In Ethiopia, a similar provision of care implementing morbidity management in health facilities worked well. However, full implementation was limited since some organizations and budgets focused only on one of the diseases at regional, zonal and districts levels (Deribe *et al*., 2017c). In a pragmatic randomized control trial in Northern Ethiopia, Lymphoedema management was implemented to prevent acute dermatolymphagioadenitis in podoconiosis patients by Negussie and colleagues. During the 12 months of follow-up, they found out that the incidence of acute

attacks was 19·4 episodes per person-year (95% CI 18·9–19·9) in the intervention group and 23·9 episodes per person-year (23·4–24·4) in the control group with an incident rate ratio of 19% (26% to 11%) significant reduction in the intervention group compared to the control group (Negussie *et al*., 2018). However, its impact on depressive symptoms and functional limitations was not assessed for a significant period such as 24 months.

2.3 Research in cognate areas relevant to the topic

Podoconiosis is totally preventable but if not managed at its early stages, it might lead to considerable physical disability, stigmatisation and economic disadvantage (Henok, 2008). Simple resource-appropriate foot hygiene regimen has proven to have considerable impact both on clinical progression and self-reported quality of life of individuals affected by filarial elephantiasis (Sikorski *et al*., 2010; Stocks *et al*., 2015). The regimen appears ideal for scaling up to other endemic regions in Ethiopia and internationally. Studies have equally shown the effects of doxycycline in reversing or stopping the progression of filarial lymphoedema (LE) in patients with LE stage 1-3 (Mand *et al*., 2012). This led to the assumption that same effect could be expected in patients with LE due to podoconiosis (PodoLE).

Some interventions for morbidity management and disability prevention in lymphatic filariasis (LF) patients with significant morbidity have shown economic benefits, reduction in disability, and improvement in their QoL. Yahathugoda and colleagues successfully evaluated the impact of a two follow-up scheme on morbidity management and disability prevention programme (a daily and monthly follow-up scheme for 14 and 13 LF participants respectively for one year) in Matara, Sri Lanka (Yahathugoda *et al*., 2018). In another pilot study, Eze and colleagues reported the effectiveness of community self-care intervention for morbidity management and disability prevention (MMDP) for

participants with leprosy, Buruli Ulcer, or LF in improving health-related QoL, decreasing disability (Eze *et al*., 2021).

2.4 Critique current literature and summary known results

Most studies having similar outcome variables (disability and depressive symptoms) were pilot studies with sample sizes less than 40 and an average duration of 12 months follow-up. The most common disease under study was LF. None of the questionnaires used in other studies (to the best of our knowledge) directly addressed the effects of morbidity management on depression which is known to be the 3rd leading cause of mental disorder and non-fatal disease burden worldwide (Sikorski *et al*., 2010; Bartlett *et al.*, 2016; Yahathugoda *et al*., 2018; Eze *et al*., 2021). However, studies done by Budge and colleagues assessed the impact of community-based lymphoedema management on the perceived disability of LF sufferers and reported a significant decrease in disability scores sustained over a period of 24 months in Orissa state, India (Budge *et al.,* 2013).

2.5 The contribution this work will make to the literature

This study will help reinforce the evidence that morbidity management reduces disability, workdays lost and more specifically depressive symptoms in podoconiosis patients following a 24 months interventional period. A clinical significant improvement due to management will help demystify misconceptions about the aetiology of the diseases hence giving room to better implement curative and preventive strategies not leaving out high compliance. This work will further help understand if there is an effect of morbidity management on workdays and how this can inferentially increase productivity at individual levels as well as boast national productivity.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Methodology

3.1.1 Study Area

The North West Region is found in the western highland of Cameroon. Its regional capital is Bamenda. It is bordered to the south west by the South West region, to the south by the West Region, to the east by the Adamawa Region and to the north by the Federal Republic of Nigeria. The region has an estimate population of 1,968,578 as censored in 2015, and a surface area of 17,300 km^2. This area has a high human density of approximately 100 to 250 people per square kilometre (Lyong *et al*., 2015).

The general climate of the North West Region has a rainy season between April and September and a dry season between October and March. Average rainfall is approximately 2400 mm and temperature average 23 °C, ranging between 15 to 32 °C. This abundant rainfall contributes to the development of agriculture and forest regeneration. This area is known on its ability to sustain high levels of biological diversity and endemicity. Three kinds of vegetation are present: lowland forest, mountain forest, and afro-alpine vegetation. The main ethnic groups are of Tikar origin, and agriculture is their main occupation (Fongnzossie *et al*., 2020).

This study was carried out at the Bamenda Clinical Trial Center (BCTC) where lymphoedema cases due to podoconiosis are being managed. The Center is situated at Foncha Street Nkwen in Bamenda headquarters of the North West Region of Cameroon as illustrated on figure 3. It is located 366 km northwest of the country's capital, Yaoundé and it lies between latitude 5° 4′ and 7° 15′ north and longitude 9° 30′ and 11° 15′ east

(Fongnzossie *et al*., 2020). The North West Region is made up of 19 health districts, of which participants resided in 11 of the districts. The 11 health districts are Bafut, Bali, Bamenda, Batibo, Fundong, Kumbo, Ndop, Ndu, Nkambe, Santa and Tubah (Ndzeshang *et al*., 2020).

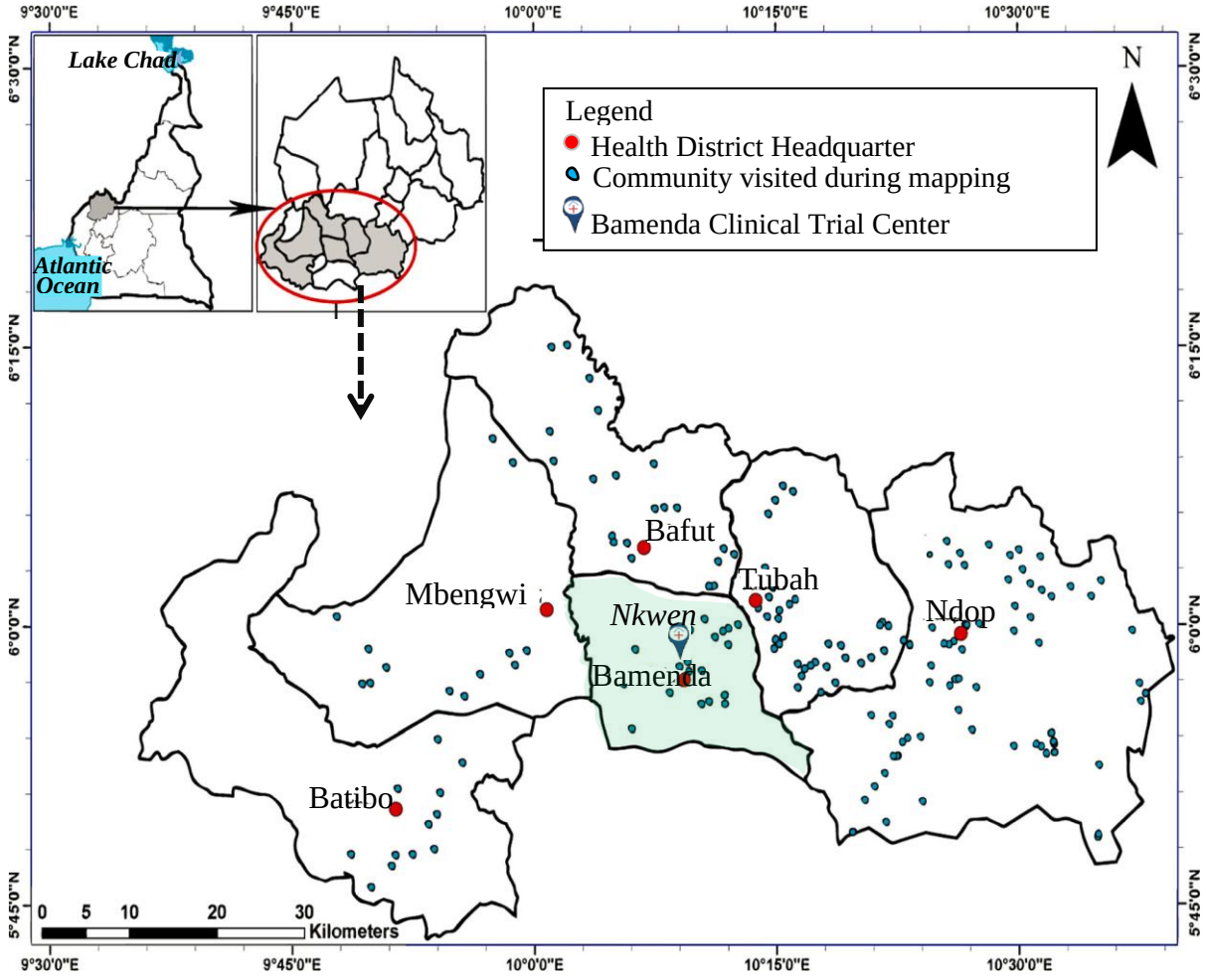


Figure 3: Study site Nkwen - Bamenda III

Source: Adapted from Wanji *et al*., 2016.

3.1.2 Study design

This was a prospective interventional study carried out at the Bamenda Clinical Trial Centre in the North West Region of Cameroon. Baseline data were collected before the intervention started. Participants were followed up for morbidity management over a

period of 24 months (endpoint) to observe or track significant functioning (disability) and depressive symptoms improvements detected by a drop in the WHODAS 2.0 and PHQ-9 scores respectively. The 12 items WHODAS II measures functional limitation (disability) while the PHQ-9 measures the depressive symptoms severity (figure 4).

A good clinical improvement in the quality of life status of a participant was characterised by a baseline decrease of at least 6 units captured by WHODAS II or a decrease of at least 5 units [18.5% of the total score (27)] of the baseline score detected by the PHQ-9 questionnaire at midline and endpoint, no acute attack occurrence from last visit and an equal or dropped in days totally unable to work or carryout usual activities in the last 30 days before assessment point (figure 4). This was done because the disability assessment schedule contains similar domains as the Short-Form 36 (SF-36) questionnaire which measures HRQoL directly. Their main difference is that WHODAS II is objective to well-being. The Patient Health Questionnaire on the other hand is subjective to well-being (since it quantifies how often participants feel or are bothered by a list of 9 items reflecting difficulties caused by the said disease two weeks before the assessment day) as does the SF-36. In addition to these two points, other studies have demonstrated that disability and depression are among the top factors that predict quality of life (Pösl *et al*., 2007; Hudson *et al*., 2008; Üstün *et al*., 2010; Diego *et al*., 2021). Tazaki and colleagues also found a significant correlation between the 12-item WHODAS II scores and that of the World Health Organisation Quality of life (WHOQoL) (Tazaki *et al*., 2014).

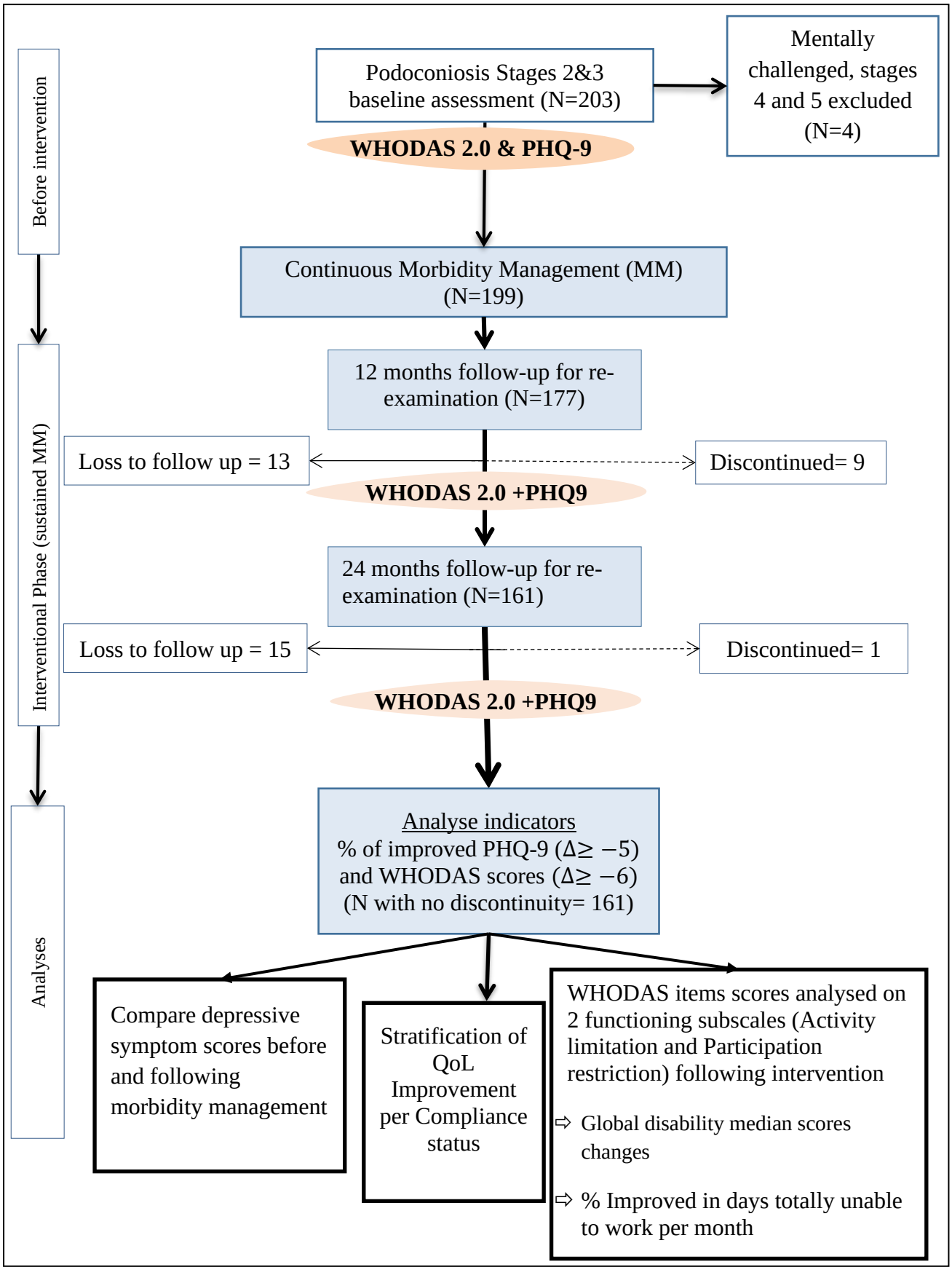


Figure 4: Flow chart of study

3.2 Sample size calculation

Based on the assumption of a regression in the disability and depressive symptoms 12 and 24 months following intervention by 30%, there will be power of 90% to show superiority to the pre-intervention time point if 140 participants are present at each follow-up assessment point (+ 30% drop-out rate: N = 200).

3.3 Research population

The population under study constituted of podoconiosis clinically confirmed cases residing in 11 of the 19 districts in the NWR for at least two years and who visited the Bamenda Clinical Trial Center. Their age ranged from 18 to 60 years. They were of either males or females and mentally sound and mature to properly respond to questionnaires willingly.

3.3.1 Recruitment of study population

Recruitment of participants was done mainly by trained Community Health Workers using both classical and short messaging services (SMS) approach. During enrolment lymphoedema specific examinations were carried out at the BCTC. Participants eligible for the trial were followed up for a 24 months period with the interventional package in which foot care and foot hygiene were paramount. At first, the main center for this study was located in Bafut but due to the greater intensity of the socio-political crises there, it was transferred to Mile 3 Nkwen at Foncha Street where most of the above activities took place. While at the Center, many other measurements were taken including tape measurements, lymphaTech scan, vital signs, urinalysis, pregnancy test, functional outcomes, depressive symptoms and hygiene assessment questionnaire administration.

3.3.2 Eligibility criteria

3.3.2.1 Inclusion criteria

Participants eligible for the study complied with all of the following:

⇨ Lymphoedema of at least one leg stage 2-3 measured on a 5-point scale

⇨ Age from 18 to 65 years

⇨ Men or non-pregnant women

⇨ Negative pregnancy test

⇨ Ability to use established standardised methods of hygiene and effectively applying it prior to the initiation of the treatment

⇨ Negative test for lymphatic filariasis (LF).

⇨ Participants who successfully completed 12 and 24 months assessment of WHODAS II and PHQ-9.

3.3.2.2 Exclusion Criteria

⇨ Patients were ineligible to participate in the study, if they had lymphoedema due to other conditions or diseases like lymphatic filariasis and HIV Aids,

⇨ Aged below 18 or above 65 years, body weight lower than 40 kg,

⇨ Any significant condition (including medical and psychological/ psychiatric disorder) which in the opinion of the study investigator might interfere with the conduct of the study,

⇨ Finally participants who did not complete all 3 assessments were excluded.

3.4 Ethical Considerations

Ethical approval was obtained from the National Ethics Committee for Health Research on Humans (CNERSH). Information about the study was given to all potential participants in a language they understood best, after which they read and signed an informed consent form. Data was collected in line with medical secret. Only identification codes were used for data treatment and results were exploited solely for scientific purposes. As such the basic ethical principles such as confidentiality with protection of personal identifiable information (PII), voluntary participation, respect for persons and non-malfeasance was observed.

3.5 Instrumentation

3.5.1 Disability instrument

Assessment of functioning quantitatively in a standardised way was an ambitious goal of the World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0). The questionnaire was pretested in several settings for various events. WHODAS 2.0 was developed as a generic assessment instrument for health and disability that could be used across all diseases, and in different population settings. WHODAS was based on the International Classification of Functioning, Disability and Health (ICF), producing standardised numeric disability levels and profiles (Üstün *et al*., 2010).

There are two methods used to score WHODAS 2.0. Based on the peculiarities of each scoring method, both simple scoring system (used to compare general disability changes with time), and Item Response Theory based scoring system (which gives a fine-grained analyses in each domain by differentially weighting the items and compares sub-groups in the study) were used in this study. The subgroups were used to display results in the format prescribed by WHO Health and Disability Manual (Üstün *et al*., 2010).

3.5.2 Depressive symptoms instrument

The Patient Health Questionnaire (PHQ-9) is a standardised, validated 9-item questionnaire used to assess symptoms of depression experienced in the 2 weeks preceding administration in adults and by extension Quality of Life (QoL). It is strongly linked with both psychiatric symptom severities as well as multiple measures of impairment subjected to feelings due to a health condition, as such podoconiosis (Kroenke *et al.*, 2001).

The PHQ-9 was used in this study to classify participants into the following categories per PHQ-9 cut-off scores (total scores range; 0 to 27): none to minimal depression (0-4), mild depression (5-9), moderate depression (10-14), moderately severe depression (15-19), and severe depression (20 and above). The last section of the PHQ-9 summarises QoL in different categories of days bordered based on difficulties faced such as working, taking care of things at home, or getting along with other people. Based on its validity and good psychometric properties across several studies and its extended use as the primary diagnostic tool for depressive disorders (major and other depressive disorders), the questionnaire best fitted the context of this study (Becker *et al*., 2002; Adewuya *et al*., 2006).

3.5.3 Data collection and scoring methods

The 12-item WHODAS has been found to be reliable, and has been reported to explain 81% of the overall variance of results of the 36-item. It has also been reported to be unidimensional, which means it defines one major concept: ‘general disability’. Saltychev and colleagues reported that it is however unclear if the 12-item version also adequately measures the same six domains as the 36-item version. It is possible that this six domain assembly has been distorted during the process of simplification (Saltychev *et al*., 2017). However, other published articles when assessing the construct of the 12-item WHODAS

2.0, used an item-response-theory (IRT) scoring method while considering the feasibility and presence of the six-factor structure of the 36-item version (Andrews *et al*, 2009; Luciano *et al*, 2010; Carlozzi *et al*, 2015; Jordans *et al*, 2020). Thomas and colleagues in their brief report captioned "The 12-item WHO Disability Assessment Schedule II as an outcome to measure for treatment of common mental disorders" also used an Item Response Theory or subscale (complex) scoring method to evaluate items in the six stated domains with much detail providing a foundational step in the development of a common disability metric for evaluating mental health treatment outcomes (Thomas *et al*, 2016). More to that, (Yang *et al*, 2020) in comparison of the responsiveness of the WOMAC (Western Ontario and McMaster Universities Osteoarthritis index) and the 12-item WHODAS 2.0 in patients with Kashin–Beck disease used IRT or complex scoring method in their research to bring out details in each domain in the tools used. These six domains were further contracted into two main subscales which resulted from exploratory factor analysis as a two factor structure of the 12-item WHODAS II illustrated in section 2.3.4 (Abedzadeh *et al*., 2016).

The baseline study was conducted from March to December 2019 and each of the 38 treatment cohort had a defined window within the stated interval. After baseline data was collected, treatment (morbidity management) ran from May 2019 to March 2022 with each cohort having an interval of 2 months per visit so as to follow up participants effectively at 12-month and at intervals of 6 months for the second year (24-month). Data for disability and depression were collected at baseline (before the intervention), 12 months follow up and finally at 24 months from treatment onset.

The 12-item version of World Health Organisation Disability Assessment Schedule (which assesses difficulties faced 30 days prior to interview day on a 5 likert response scale) and the Patient Health Questionnaire (PHQ-9) instruments were administered

before (at baseline) and following intervention (at 12 and 24 months) to collect data (figure 4). WHODAS 2.0 and PHQ-9 instruments were interviewer-administered. Interviews were done in English language, none the less if participants had difficulties understanding, further probing was done in Pidgin English. WHODAS 2.0 took 10 to 15 minutes depending on the participant's understanding of the items in each domain while PHQ-9 instrument took approximately 5 minutes.

The WHODAS scoring is coded from 0 to 4 (5-point Likert-scale) corresponding respectively to "none", "mild", "moderate", "severe" and "extreme" difficulty. Accordingly, the lowest and the highest possible scores of the WHODAS II were 0 and 48, respectively. Higher scores reflect higher levels of difficulty (by extension poorer degrees of quality of life related to podoconiosis). All demographic data in the study were collected using the questionnaire. After administering the questionnaire, a simple scoring method was used where the scores assigned to each item are summed up and converted to a metric ranging from 0 (no disability) to 100 (full disability) with higher scores indicating more severe disability (0-4 indicates no difficulty, 5-24 indicates mild difficulty, 25-49 indicates moderate difficulty, 50-95 indicates severe difficulty, and 96-100 indicates extreme difficulty) (Üstün *et al*, 2010; Wolf *et al*., 2012). The stated formula was used to convert the scores from a total of 48 to a 100;

[(Actual score) / (Maximum score) * 100] (Abedzadeh *et al*., 2016).

The formula syntax for simple scoring method was then inserted in Excel as;

St_S12 = SUM (S1:S12)*100/48

Where; St_S12 = sum total of all 12 unweighed items.

An IRT based scoring which consists of differentially weighting items using computer softwares (SPSS and Ms excel) was used to give a fine-grained analyses of the 6 domains (a pair of related questions per domain) in the questionnaire and to compare subgroups

while taking into account multiple levels of difficulty due to podoconiosis. Basically, the recorded items within each domain were summed up after a differential recoding was done. All related item scores were summed and then converted to a metric ranging as described in the WHODAS manual for health and disability (Üstün *et al*, 2010).

St_S12d = SUM (S1:S12)*100/38.

Where**;** St_S12d is the sum total of 12 differentially weighed items

- **Dom1 = (S3+S6)*100/8**
- **Dom2 = (S1+S7)*100/8**
- **Dom3 = (S8+S9)*100/6**

Sg_Al =(S1+S3+S6+S7+S8+S9)*100/22

- **Dom4 = (S10+S11)*100/4**
- **Dom5 = (S2+S12)*100/6**
- **Dom6 = (S4+S5)*100/6**

Sg_P =(S2+S4+S5+S10+S11+S12)*100/16

Where;

Dom1 = Cognition domain

Dom2 = Mobility domain

Dom3 = Self-care domain

Dom4 = Getting along (Interpersonal) domain

Dom5 = Life activities domain

Dom6 = Participation (in the society) domain

Dom1, 2 and 3 were constituents of the Activity limitation Subgroup (Sg_Al) while Dom4, 5 and 6 made up the Participation restriction Subgroup (Sg_P). These equations were slightly modified from those of the WHODAS Manual measuring health and disability (Üstün *et al*, 2010). The 12 items (S1 to S12) were further grouped into two main subscales (Sg_Al and Sg_P) as stated in (Abedzadeh *et al*., 2016).

The equations were multiplied by 100 to convert the scores into a metric ranging from 0 to 100, and divided by either 8 or 6 or 4 since some items were differentially weighted.

In other words the domain items were recoded base on their psychometric properties (Abedzadeh *et al*., 2016).

The effect of difficulties in participants was also assessed by recording the days of partial and total inability to work or study as result of the debilitation impact of podoconiosis reported by participants 30 days before interview date. This section assessed the extent to which various difficulties participants encountered had affected their lives. Out of the three questions asked (H1, H2, and H3), the most indicative of these (H2) was used as a determining outcome of disability effect. H2 assessed the number of days participants were totally unable to carry out their usual activities or work because of the health condition (podoconiosis) in the last 30 days. This was deduced from H1 which generally rates all difficulties assessed in the interview.

To calculate the productive time gained in person-years over 24 months of follow up, the product of the sample size, difference in mean days lost per month and follow-up duration (in months) divided by 365days was used.

The PHQ-9 which assesses how often participants were bordered by 9 podoconiosis related health problems over the last 2 weeks was coded thus; not at all (0), several days (1), more than half the days (2) and nearly every day (3). The sum of the 9 items was then recorded which ranged from 0 to 27. The participants were then categorised into 5 groups (none to severe depression) based on the cut-off points. The last section summarises the QoL of the participants in 4 categories which are; not difficult at all, somewhat difficult, very difficult and extremely difficult.

Questions from the hygiene assessment form were used to assess participant's compliance to lymphoedema management. Critical questions such as when last participants washed their affected limb(s), the frequency at which it is washed in a day, washing location, water availability, use of soap, limb position while sitting or sleeping were coded with

higher values corresponding to the correct answers. The second part of the questionnaire consisted of an independent observation of limb(s) by an interviewer. The total score for each visit was calculated and average score (sum of total score divided by number of visits) per participant was recorded. An average score of 14.0 – 24.4 was graded as poor compliance and 24.5 – 30.0 as good compliance to lymphoedema management. The cut off of 24.4 was chosen based on the mean of all scores of all participants.

3.6 Specific procedures

3.6.1 Morbidity management procedures

Morbidity management entails all practices of lymphoedema management and accessibility to management (chemotherapy and practices to reduce pain, swellings, redness and fever) of acute attacks. Lymphoedema management procedures were explained to all participants and they were trained to use established standardised methods of foot hygiene. The nurse and other health professionals at the Morbidity Management Center dispensed these instructions and practical demonstrations to participants. Lymphoedema management comprised foot hygiene and foot care. The following foot hygiene procedures were executed at the Center.

1. The affected leg(s) was soaked in water containing antiseptics (dermobacter) for 15 to 20 minutes (especially on keratinised skin);

2. Scrubbed and washed with bathroom soap (around the folds and nails) with a pH lower than 9 to minimise the effects of this soap on skin barrier function (figure 5A and B).

3. The legs were rinsed with clean water, dried and emollient (Vaseline) applied (figure 5C and D).

4. If wounds were present on leg, bandaging and socks were worn to prevent further infections (Figure 5E and F).

Finally, participants were trained on foot care which entails supervised use of single-layer, non-elastic bandages for disease stages of at least 3; foot and calf exercises (not practiced during ADLA attacks). This was followed by instructions to practice foot hygiene daily at home, to elevate the affected leg while sleeping or sitting (to ease circulation of lymph) and to use shoes during walking hours.

Figure 5: Washing routine for patients at the Center (source: Wanji *et al*., 2021)

3.6.2 Compliance to lymphoedema management

Adherence by participants to the intervention consisted of the procedures stated in 3.6.1. Participants were reminded of their hygiene measures at each contact point or visit (visit 2, 5, 6, 9, 12, and 15 which corresponded to baseline, 4-month, 6-month, 12-month, 18-month and 24-month follow-up respectively). During these visits materials or items to help support daily self-treatment (soaps, buckets, Vaseline, towels, antiseptics, socks depending on the state or stage of the leg, and gauze) were given and hygiene assessment

form was use to assess participants' compliance to lymphoedema management not leaving out independent observation from interviewer.

3.7 Treatment and Analysis of the Data

Data collected (using 12-item WHODAS II and PHQ-9, which is a section on the case report form) during visit days were double-entered in Research Electronic Data Capture (REDCap 7.0.6 -Vanderbilt University, Nashville, Tennessee, USA. https://www.project-redcap.org) software. The data was extracted from REDCap, cleaned, recoded and analysed in MS Excel 2010 (Microsoft Corporation, Redmond, Washington, USA). Further analyses were executed on IBM SPSS 25 (IBM Corp; Armonk, New York, USA), like non-parametric tests and R studio version 4.0.5 (Integrated Development for R. RStudio, PBC, Boston, MA URL), like boxplots with strip-charts. The file containing the data was coded, and only authorised research team members had access to the password of the encrypted file.

3.7.1 Research variables

3.7.1.1 Dependent variables

Outcome variables were disability and depressive symptoms scores changes following measure sequence.

3.7.1.2 Independent variables, factors and other Predictors

In this study, our fixed factor was lymphoedema management compliance status. Other factors such as gender, occupation, marital status, educational duration, were analysed to see if they are significantly associated to changes in outcome variables. Age and educational duration were important covariates in the study.

3.7.2 Statistical Analysis

The Chi-square test was used to analyse distributions and variations of demographic data from which variables such as gender, educational duration, occupation, presence of partner, and age were coded as dummy variables (0 or 1). Odds ratios (OR) at 95% confidence interval (CI) and mean square contingency coefficient (phi) were used to measure the association and the strength of the relationship between socio-demographic variables and study outcomes at each time point respectively. A test of normality was carried out using the one sample Kolmogorov-Smirnov test. The differences in WHODAS 2.0 scores between 12-month or 24-month and baseline were normally distributed. Unlike the disability score differences, normality test revealed that changes in PHQ 9 at midline and endpoint from baseline were not normally distributed though Skewness was close to 0. Since normality was violated in one of the assessment score changes, the Wilcoxon signed-rank test was used to compare the scores obtained at baseline to those generated at 12 (midline) and 24-month (endpoint) follow up. The Mann-Whitney U test was also used to determine if there was any significant difference in the lymphoedema management compliance strata and outcomes variables. In order to account for repeated measurement overtime, a linear mixed effect model that fits in assessment time and compliance status in the mixed-design ANOVA (analysis of variance) was used. Multivariate test was executed on generalised linear model to investigate the relationship between categorical variables, possible predictors and study outcomes. All tests were 2 tailed with a significance (some adjusted by Bonferroni correction to limit type I errors) level set at $p < 0.05$.

3.8 Scope of the current study

This research is set to assess the effects of morbidity management on the disability and depressive symptoms of podoconiosis patients within the North West Region of

Cameroon with highest stage number being 2 or 3 and who have lived in the NWR for at least 2 years. There was no direct measurement of the quality of life nevertheless strong predictors such as functional limitations, days totally unable to carryout usual activities, depressive symptoms, and acute attack occurrence were used to detect clinical improvement status of QoL based on cut-off points. Only functional limitations and depressive symptoms related to podoconiosis were assessed 30 days prior to interview day. Outcome variables measurements were limited at 3 time points; baseline, 12 and 24 months following the intervention. Daily assessments of lymphoedema management compliance were not possible due to socio-political crises and the frequency of visits during the first 12 months was higher than those from 12 to 24 months follow up.

CHAPTER FOUR

RESULTS

4.1 Socio-Demographic characteristics of study participants

A total of 200 participants were eligible for the study but we could not administer WHODAS and PHQ-9 questionnaires to one participant who was mentally derailed. Out of the 199 participants, 177 (88.9 %) were interviewed at midline and a dropout rate of 11.1 % was recorded (between baseline and midline, 13 participants were lost to follow up, and 9 discontinued). Of the 177 participants at midline, 161 (91.0 %) continued at 24-month visit with a dropout rate of 9 % (between midline and endpoint, 15 participants were lost to follow up and 1 discontinued).

4.1.1 Gender Distribution of study participants

Of the 199 participants, 177 (89 %) were female and 22 (11 %) were male (figure 6).

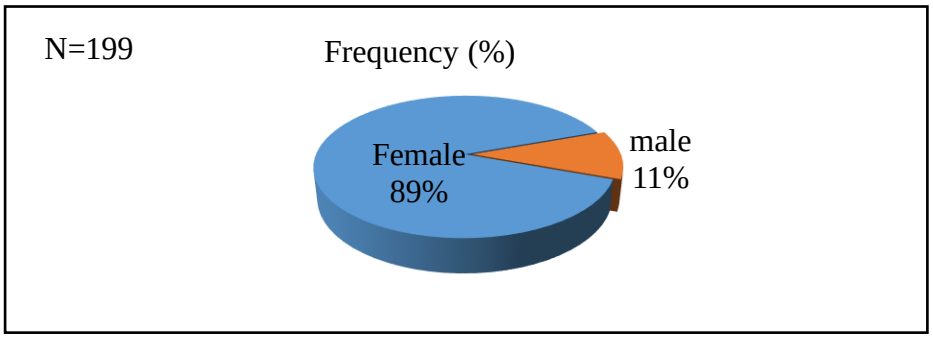


Figure 6: Distribution of study participant by gender

4.1.2 Marital status of participants

Out of 199 participants 91 (45.5%) were married, 47 (24.3%) were never married, 29 (14.7%) were widowed, 13 (6.5%) were cohabiting, 8 (4.0%) separated and 11 (5.0%) divorced (figure 7). Participants separated from partners had the highest median disability score of 32.4 (with a 25th-75th percentile of 28.6-56.7) at baseline and those who never

got married demonstrated the lowest scores with a median of 27.8 (25th percentile of 10.5 and 75th percentile of 37.1) (figure 8).

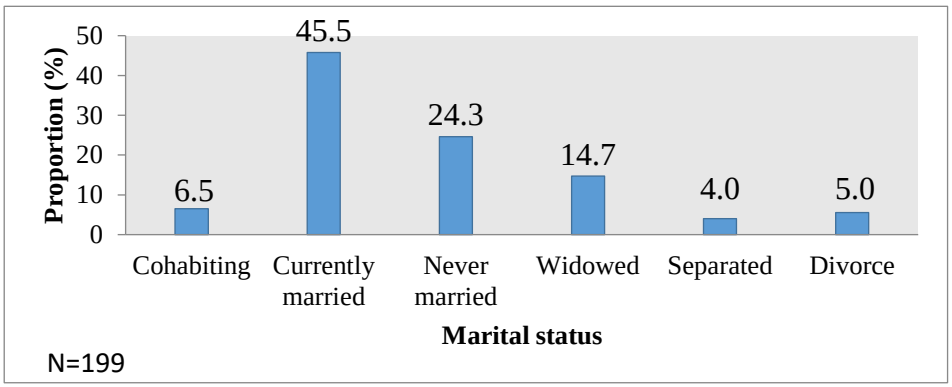


Figure 7: Marital status of study participants the study

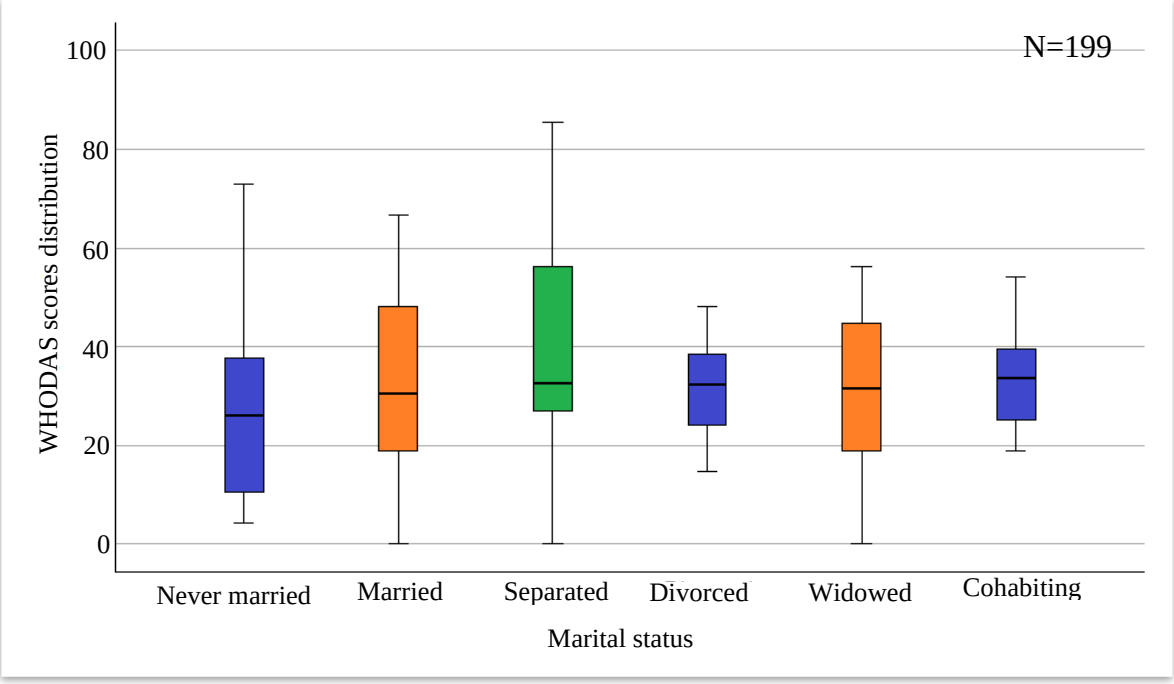


Figure 8: Perceived disability score distribution at baseline per marital status

4.1.3 Educational duration

The average years spent in school at baseline was 9.6 (standard deviation of 6.1). Out of 199 participants, 18(9.04%) participants did not go to school at all, 76(38.19%) made at most 7 years, 35 (17.60%) fall within the range of 8 – 15 years, and 70 (35.17%) participants fall within the educational duration range of 16 – 25 (figure 9).

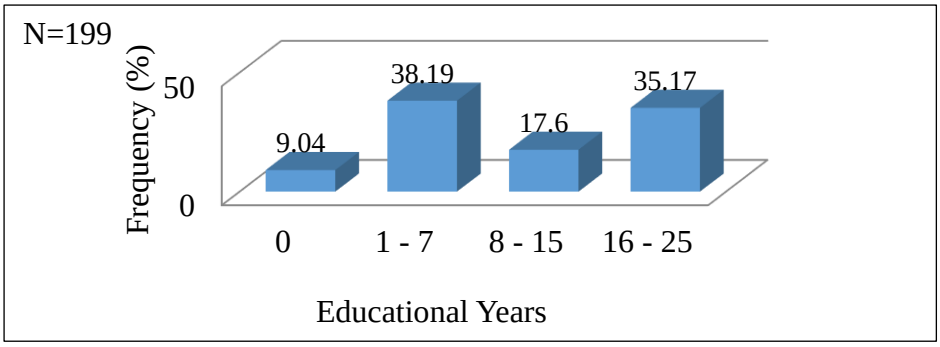


Figure 9: Distribution of study participants per school years

4.1.4 Age group and participants occupation

The age category of participants enrolled in the study ranged from 18 to 64 years, with a mean age of 42.5 and a standard deviation (SD) of 11.77 years. Of the 199 participants at baseline, 85(42.7%) were of the age group 18 to 40 years and above 40 years, 114(57.3%) participants did belong. Out of 199, 154(77.4%) were farmers and self-employed participants, 25(12.6%) were employed by private or public sectors (paid work), 15(7.5%) were students and the rest 5(2.5%) could fall under one of the following categories; house wife, retired, or unemployed (table 2).

Table 2: Distribution of age group and occupation of podoconiosis participants

	Study subjects (N=199)	**n (%)**	**Mean age (±SD)**
Age group (years)	18-30	36 (81.1)	**42.5 (11.77)**
	31-40	49 (24.6)	
	41-50	53 (26.6)	
	51-64	61 (30.7)	
Occupation	Self-employed (Business or Farming)	154 (77.4)	———
	Paid work	25 (12.6)	
	Student	15 (7.5)	
	Home maker	1 (0.5)	
	Retired	2 (1.4)	
	Unemployed	1 (0.5)	
	Unemployed (other reasons)	1 (0.5)	

4.1.5 Baseline disability and depressive symptoms scores

Out of the 199 participants, 108(54.2%), 110(55.2%), and 110(55.2%) participants had severe disability in the mobility, life activity and participation domain respectively (figure 10). At baseline, 45% of the participants had mild depression and 21.3 % had moderate to moderately severe depressive symptoms (figure 11).

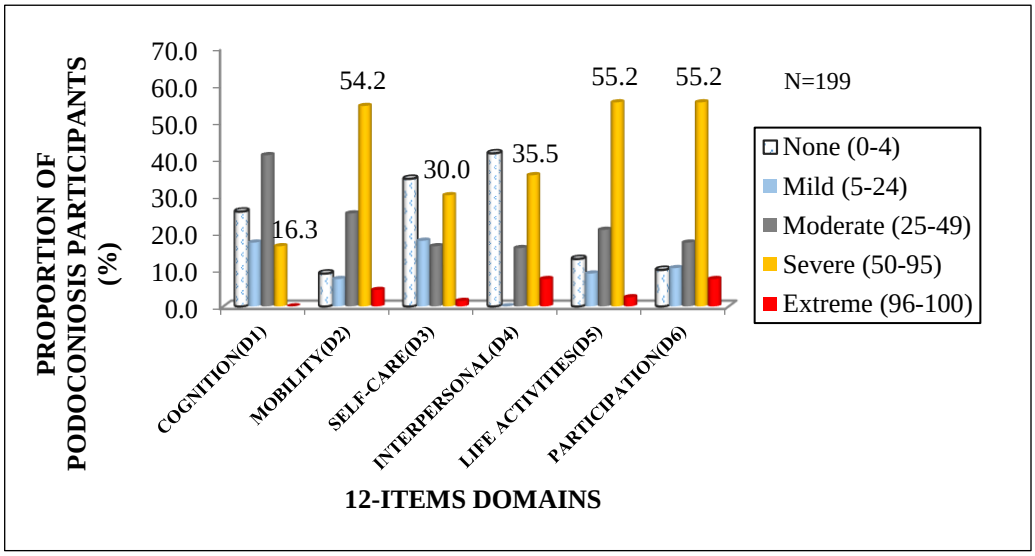


Figure 10: Percentage of podoconiosis participants' perception on difficulty levels across the six disability domains at baseline

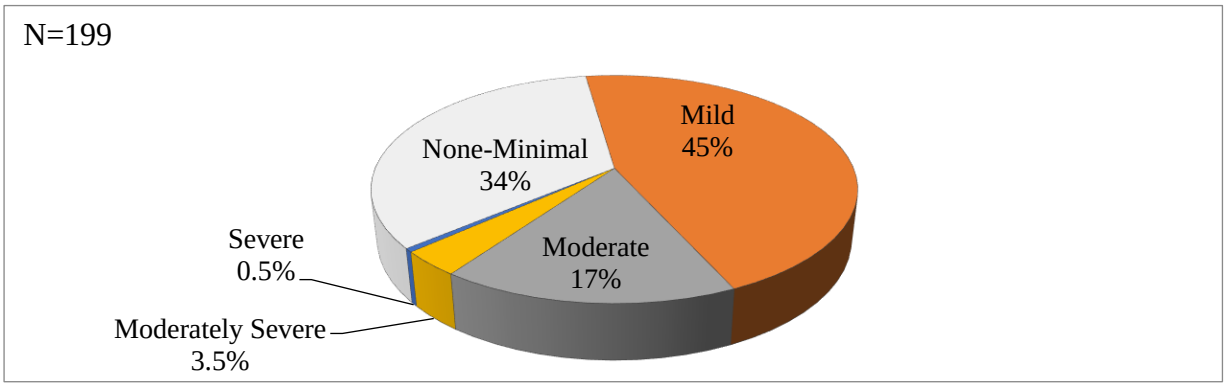


Figure 11: Proportions of podoconiosis participants' depressive symptoms severity at baseline

4.1.6 Effect of morbidity management on the association between functional limitations and depressive symptoms in socio-demographic subgroups following measure sequence

4.1.6.1 Effect of morbidity management on the association between demographic variables and functional limitations (disability)

Chi square test was used to evaluate the association between functional limitations and demographic variables. The disability status at baseline did not vary significantly according to demographic characteristics (all $p > 0.05$). However, There was a significant association between employment status and functional limitation at midline ($p = 0.038$) where the odds of having functional limitation amongst farmers was more than two times higher than that of other professions with an OR (CI) of 2.23 (1.04 – 4.81). There was no significant association at endpoint ($p = 0.055$). The strength of the association got weaker (turning to no association) from midline to endpoint with a phi nominal by nominal value of 0.164 and 0.151 respectively (table 3).

Table 3: Socio-demographic association with functional limitation following intervention

N = 161	Baseline (n(%))		12-month follow up (n(%))		24-month follow up (n(%))	
Demographic variables	F.L	No F.L	F.L	No F.L	F.L	No F.L
			Sex			
Female	139(95.0)	7(5.0)	90(61.6)	56(38.4)	114(78.5)	32(21.9)
Male (ref)	15(100.0)	0(0.0)	6(40.0)	9(60.0)	10(66.7)	5(33.3)
p-value	1.00[f]		0.177[cc]		0.338[f]	
			Living with Partner			
Yes	76(96.2)	3(3.8)	52(65.8)	27(34.2)	62(74.1)	22(25.9)
No (ref)	78(95.1)	4(4.9)	44(53.7)	38(46.3)	61(80.3)	15(19.7)
p-value	1.00[f]		0.116[p]		0.67[p]	
			Age (years)			
18-44	82(96.5)	3(3.5)	46(54.1)	39(45.9)	63(74.1)	22(25.9)
45-62 (ref)	72(94.7)	4(5.2)	50(65.8)	26(34.2)	61(80.3)	15(19.7)
p-value	0.708[f]		0.089[p]		0.355[p]	

N = 161	Baseline (n(%))		12-month follow up (n(%))		24-month follow up (n(%))	
Demographic variables	F.L	No F.L	F.L	No F.L	F.L	No F.L
Educational duration (years)						
0-9 (ref)	90(95.7)	4(2.3)	59(62.8)	35(37.2)	73(77.7)	21(22.3)
10-22	64(95.5)	3(4.5)	31(58.5)	22(41.5)	51(76.1)	16(23.9)
p-value	0.685[f]		0.336[p]		0.819	
N[0] Affected Leg(s)						
Both (stage2 & or 3)	104(96.3)	4(3.7)	65(60.2)	43(39.8)	88(81.5)	20(18.5)
One (stage 0 & or 1) ref	50(94.3)	3(5.7)	31(58.5)	22(41.5)	51(76.1)	16(23.9)
p-value	0.685[f]		0.837[p]		0.055[p]	
Employment status						
Farmer/Self-employed (ref)	121(95.3)	6(4.7)	81(63.8)	46(36.2)	102(80.3)	25(19.7)
Others	33(97.1)	1(2.9)	15(44.1)	19(55.9)	22(64.7)	12(35.3)
p-value(OR,CI)	1[p]		**0.038[p](2.23,1.04-4.81)**		0.055[p]	

Ref: reference group, OR: Odds ratio, CI: Confidence interval, F.L: Functional limitation, [p]: Pearson chi-square, [cc]: continuity correction, [f]: fisher's exact test, N**: Number of participants, n: frequency**

4.1.6.2 Association between demographic variables and depressive symptoms following measure sequence

There was a general drop in the proportion of podoconiosis participants having at least mild depression following measure sequence (strength of the nominal by nominal association value was relatively higher at baseline compared to midline and endpoint) in the demographic variables. There was no significant association between gender and depression [(p = 0.26 at baseline, 0.75 at 12-month, 0.78 at 24-month) and the strength of the association turned to 0 from baseline (phi = 0.1) to midline (phi = 0.03) and endpoint (phi = 0.03)], marital status [(p = 0.25, 0.28, 0.86) with their respective assessment points phi values of -0.09, -0.08, and 0.01 demonstrating a shift to a weaker negative association] and depression (table 4).

There was however a significant association between depressive symptoms and the elderly of 45 years and above at baseline (p = 0.03) with an odds ratio of 2.06. The strength of association was negatively weak at baseline (phi = -0.17) though turning to no association at 12 (phi = -0.11) and 24-month (phi = -0.13) (table 4).

The odds of having depressive symptoms was more than two times higher amongst those with lesser school years (0 – 9) following measure sequence (OR at baseline; 2.03, at midline; 2.73 and at endpoint 2.06). The strength of the association varied from (positive) moderate to very weak following measure sequence (phi = 0.26, 0.19, and 0.16) (table 4).

The odds of depressive symptoms in farmers/self-employed podoconiosis participants at baseline were 5.1 times higher compared to those in other professions with a significant association of p < 0.001; this odd dropped from 5.1 to 2.6 and 2.1 over time. The strength of the association declined from a moderately positive strong relationship (phi = 0.33) at baseline to a positive very weak relationship (phi = 0.14, 0.05) at 12 and 24-month following intervention (table 4).

Table 4: Demographics and Depressive symptoms (DS) proportions following intervention (N = 161)

	Baseline (n(%))		**12-Month follow up (n(%))**		**24-Month follow up (n(%))**	
Variables	DS	No DS	DS	No DS	DS	No DS
			Sex			
Female	93(63.7)	53(36.3)	33(22.6)	113(77.4)	46(26.7)	11(73.3)
Male (ref)	12(80.0)	3(20.0)	4(26.7)	11(73.3)	4(26.7)	11(73.3)
p-value(OR,CI)	0.263[f] (2.28, 0.60-8.40)		0.750[f]		0.779[f]	
			Living with Partner			
Yes	55(69.6))	24(30.4)	21(26.6)	58(73.4)	24(30.4)	55(69.6)
No	50(61.0)	32(39.0)	16(19.5)	66(80.5)	26(31.7)	56(68.3)
p-value	0.25[p]		0.28[p]		0.86[p]	

	Baseline (n(%))		12-Month follow up (n(%))		24-Month follow up (n(%))	
Variables	DS	No DS	DS	No DS	DS	No DS
Age (Years)						
18-44	49(57.6)	36(42.4)	16(18.8)	69(81.2)	22(25.9)	63(74.1)
45-62	56(73.7)	20(26.3)	21(27.6)	55(72.4)	28(38.8)	48(63.2)
p-value(OR,CI)	**0.033[p] (2.06, 1.06-4.01)**		0.185[p] (1.65, 0.69-3.45)		0.134[p] (1.67, 0.85-3.27)	
Educational duration						
0-9 (ref)	71(66.7)	34(50.7)	28(29.8)	66(70.2)	35(37.2)	59(62.8)
10-22	34(50.7)	33(49.3)	9(13.4)	58(86.6)	15(22.4)	52(77.6)
N[0] of Affected leg(s)						
Both	72(66.7)	36(33.3)	24(22.2)	84(77.8)	34(31.5)	74(68.5)
One	33(62.3)	20(37.7)	13(24.5)	40(75.7)	16(30.2)	37(69.8)
p-value	0.582[p]		0.744[p]		0.860[p]	
Employment status						
Farmers/Self-employed(Ref)	93(73.2)	34(26.8)	33(26.0)	94(74.0)	41(32.3)	86(67.7)
Others	12(35.3)	22(64.7)	4(11.8)	30(88.2)	9(26.5)	25(73.5)
p-value(OR,CI)	**<0.001[p] (5.01, 2.24-11.22)**		0.108[f] (2.63,0.86-8.04)		0.659[cc]	

4.2 Effect of intervention on disability and incapacitated days over assessment time

4.2.1 Differences in activity limitation and participation restriction subscales

The activity limitation at baseline mean score (SD) was 34.1(20.2), which decreased to 14.9(15.8) at 12-month and to 17.7(16.7) at 24-month following intervention. The participation restriction subscale mean (SD) at baseline dropped remarkably from 39.3(21.3) to 3.1(3.1) at midline and subsequently increased to 22.6(18.9) at endpoint (figure 12).

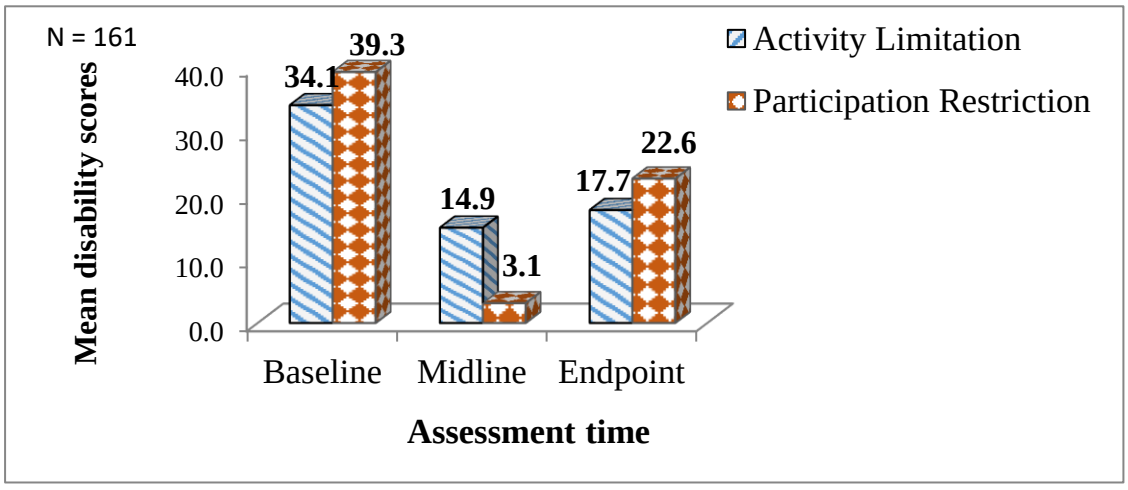


Figure 12: Mean activity limitation and participation scores following intervention

4.2.2 Differences in overall disability in podoconiosis participants over time

The overall or general disability median (IQR) decreased significantly from 31.3 (18.8, 45.4) at baseline to 8.4 (2.7, 18.7) at midline and to 14.6 (6.4, 27.6) at endpoint ($p < 0.05$) using Wilcoxon signed-rank test (figure 13B). The proportion of podoconiosis participants with no disability remarkably increased from 1.9% at baseline to 30.4% at midline and 18.6% at endpoint (figure 13A).

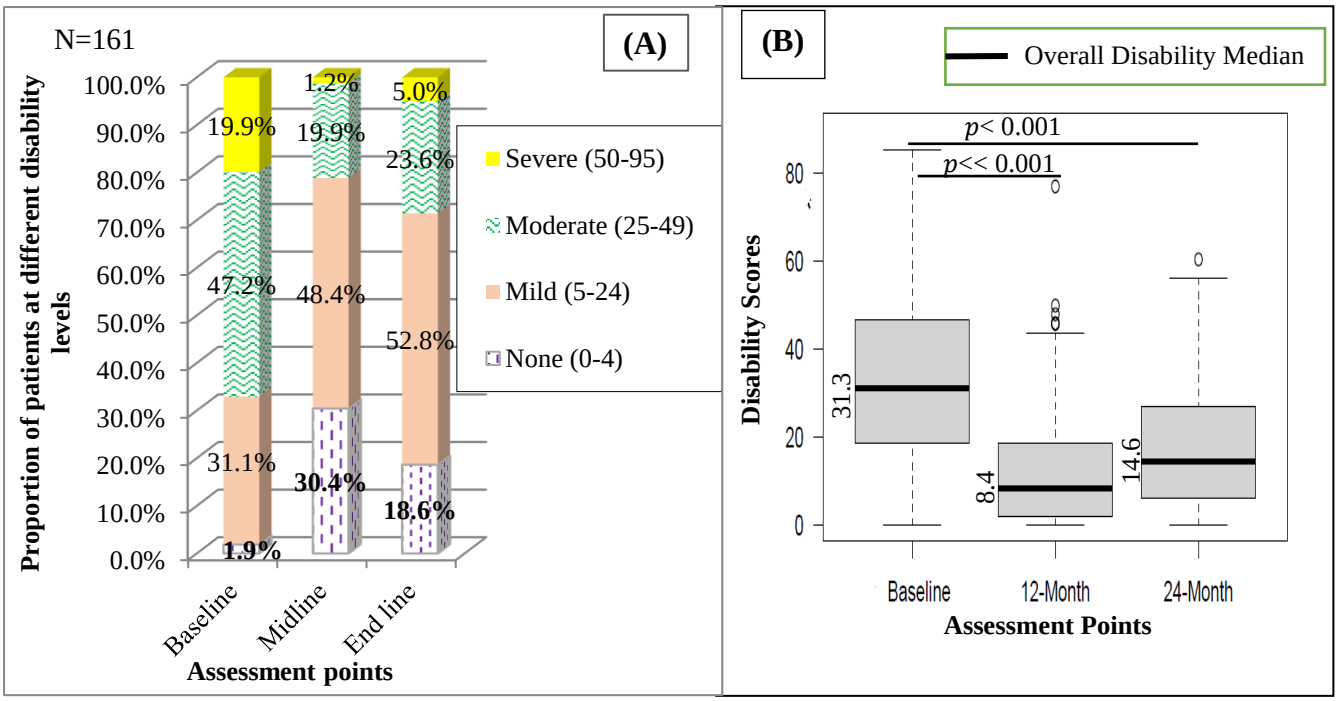


Figure 13: Proportions of participants' disability severity (A); and overall disability median (B) differences following measure sequence

4.2.3 Differences in days of work lost (incapacitated days)

There was an increase in the proportion of participants who had not lost a working or schooling day from baseline (49.7%) to 12-month (73.3%) and 24-month (70.2%) (figure 14A). The mean days of work lost due to podoconiosis dropped from 2.5 at baseline to 1.3 at midline and endpoint (figure 14B). The median workdays lost (IQR) decreased significantly ($p<0.001$) from 1 (0, 3.8), to 0 (0, 1) (figure 14C).

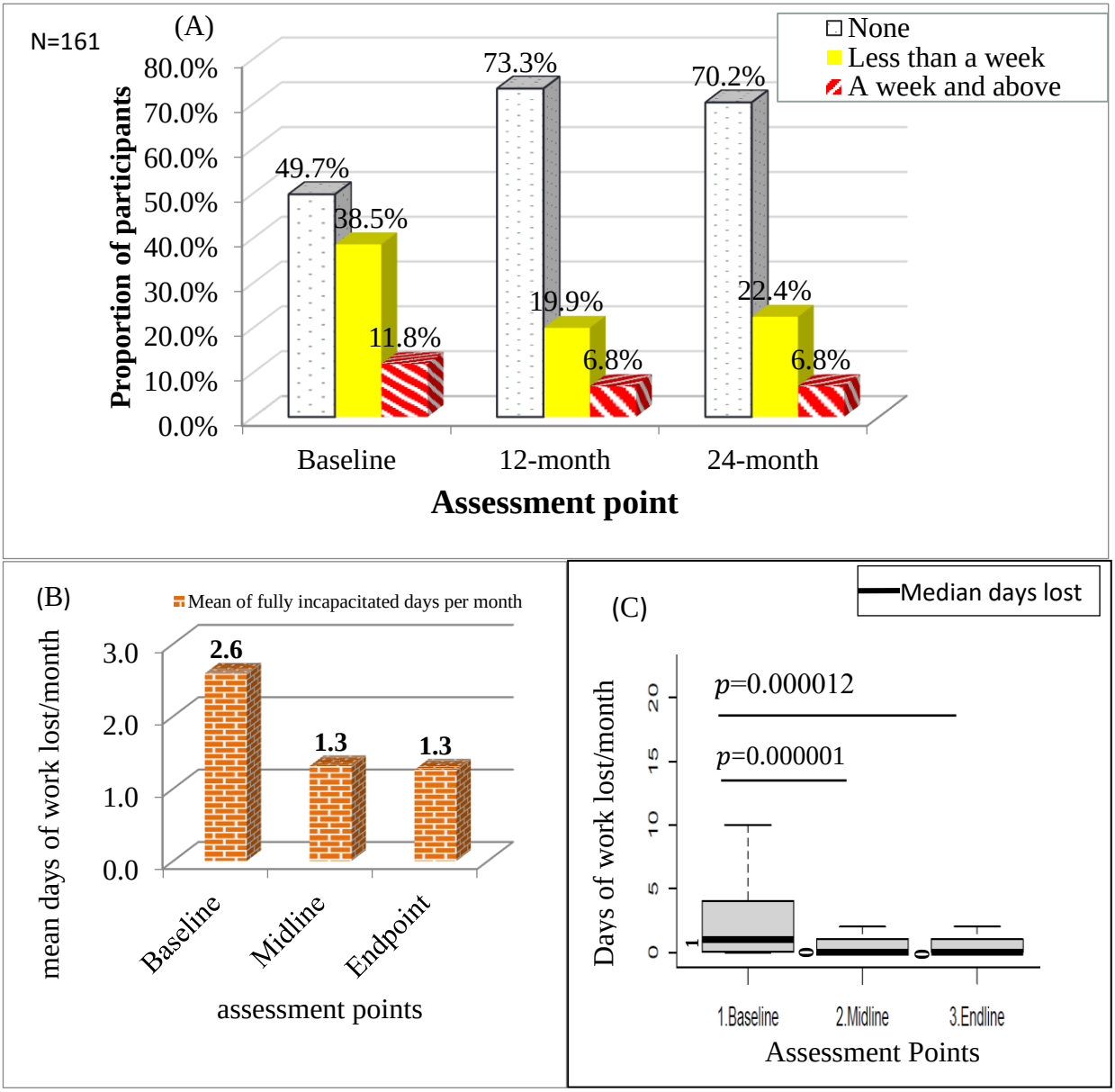


Figure 14: Differences in proportions (A), average days of work or activity lost (B) and Box plot median differences (C)

4.2.4 Comparison between functioning domains following measure sequence

Overall, there was a statistically significant decrease comparing 12 and 24-month to baseline median ($p<0.05$). The cognitive, self-care, interpersonal, and participation domains showed a consistence significant decrease ($p < 0.001$) at 12 and 24-month when

compared to their respective baseline medians (25^{th}, 75^{th} percentiles) of 25.0 (0.0, 37.5), 16.7 (0.0, 50.0), 50.0 (33.3, 66.7) (table 5).

Table 5: Differences in median (IQR) domain scores following measure sequence

N = 161	**Baseline**	**12-month**	**24-month**	
Domains	Median(IQR)	Median(IQR)	Median(IQR)	p-values
Cognition(D1)	25.0(0.0-37.5)	0.0(0.0-12.5)	0.0(0.0-12.5)	<0.001
Mobility(D2)	50.0(25.0-68.8)	12.5(0.0-50.0)	25.0(6.3-50.0)	<0.001
Self-care(D3)	16.7(0.0-50.0)	0.0(0.0-16.7)	0.0(0.0-33.3)	<0.001
Interpersonal(D4)	25.0(0.0-50.0)	0.0(0.0-0.0)	0.0(0.0-0.0)	<0.001
Life activities(D5)	50.0(16.7-66.7)	0.0(0.0-33.3)	16.7(0.0-33.3)	<0.001
Participation(D6)	50.0(33.3-66.7)	16.7(0.0-33.3)	16.7(0.0-50.0)	<0.001

D: domain, IQR: Inter Quartile Range, N: number of participants who completed the study, P-value: compares midline and endpoint to baseline (significant at $p<0.05$)

4.3 Effect of morbidity management on depressive symptoms in podoconiosis participants

The mean depression score at baseline was 6.5 and this dropped to 2.9 and 3.4 at 12 and 24-month respectively (figure 15A). A statistical significant decrease was recorded ($p< 0.001$) as the median (25^{th}, 75^{th} percentiles) dropped from 6.0(3.0, 9.0) at baseline to 2.0(0.0, 4.0) and 3.0(1.0, 5.0) at midline and endpoint respectively using Wilcoxon signed-rank test (figure 15B). There was an increase in the proportion of podoconiosis participants with no depressive symptoms from 35% at baseline to 77% and 69% at midline and endpoint respectively (figure 16).

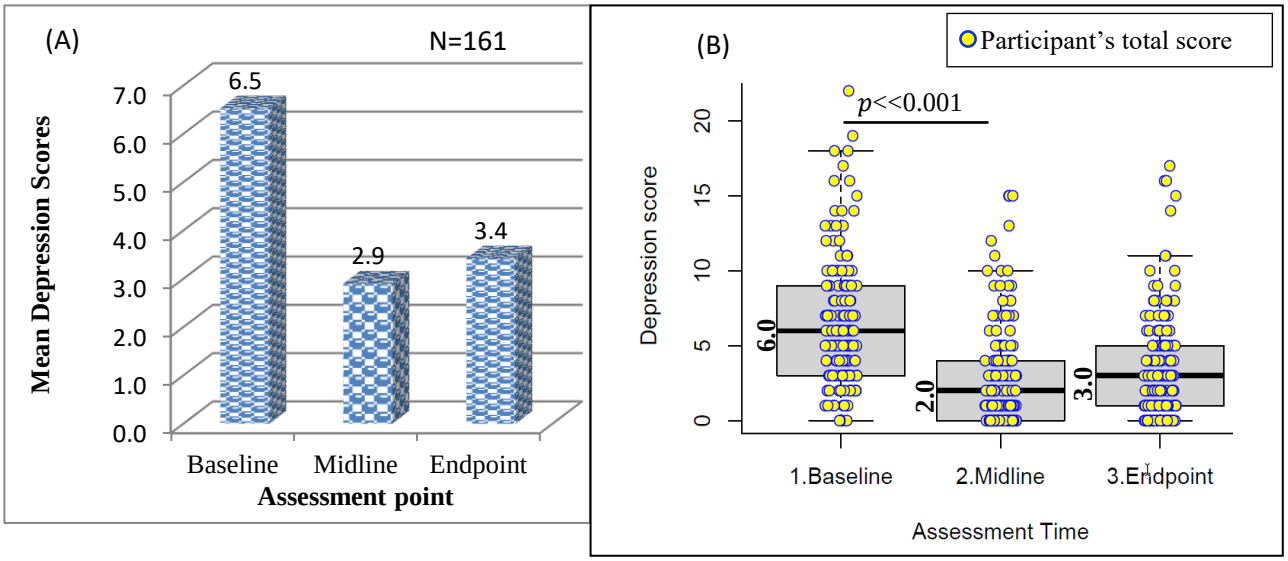


Figure 15: Comparison of mean depressive symptoms scores at 12 and 24-month (A). Box plot showing significant differences (B)

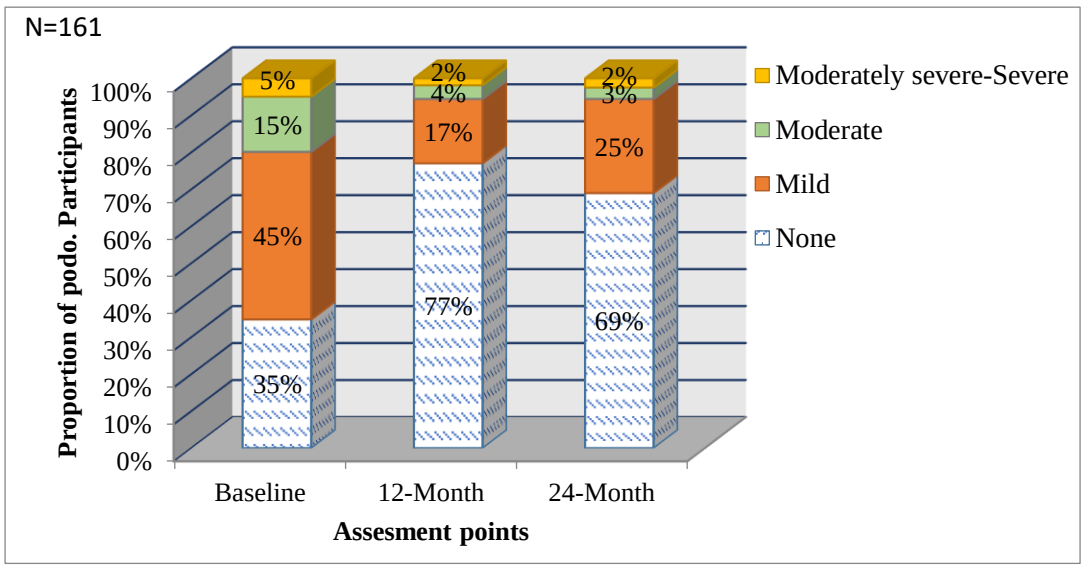
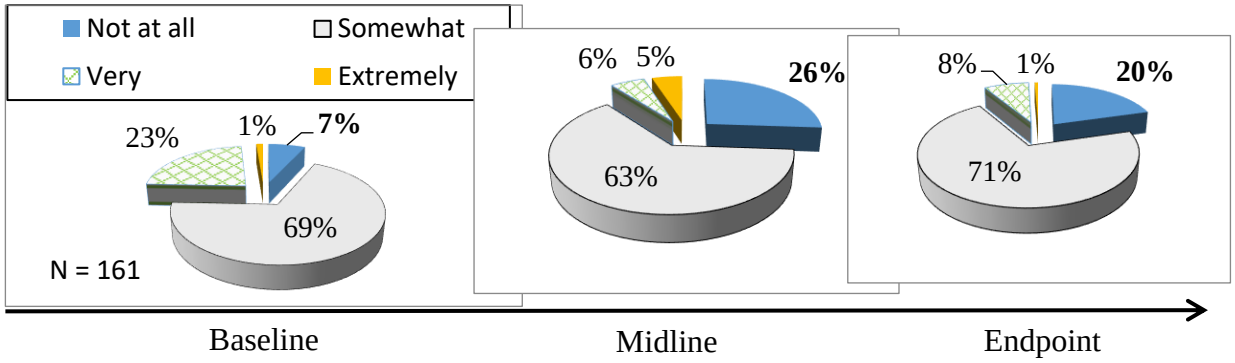


Figure 16: Changes in depression severity proportions following measure sequence

The overall QoL related to depression due to podoconiosis showed that 7% of the participants reported not to have faced any difficulty at baseline and this increased to 26% and 20% 12 and 24-month respectively following intervention (figure 17).

Figure 17: QoL summary item of the PHQ related to podoconiosis following measure sequence



4.4 Effect of lymphoedema management (LM) compliance subgroup on study outcomes in podoconiosis participants

Adherence by participants to lymphoedema management (LM) was consistently above 85% for washing limbs with soap, applying ointment, and elevation. However, adherence to instructions to elevate legs was lower especially during the first 3 visits (baseline, 4-month and 6-month). Out of 161 participants, 138 (85.7%) adhere to LM while 23 (14.3%) poorly complied. When stratified by gender, educational duration, living with partner, and highest stage; 129 (93.5%) of females, 63 (45.7%) of those who spent above 9 years schooling, 69 (49%) living with partner, and 75 (64.3%) of highest stage being stage 3 highly complied to lymphoedema management respectively. The odds of good compliance to LM were 5.2 times higher amongst females than males and 3.95 times higher amongst stage 2 than stage 3 participants. There was no significant association between compliance status and study outcome improvements when stratified by stage, sex, educational duration, and marital status at 24-month ($p > 0.05$) (table 6).

Repeated measure linear model analysis showed age to be significantly associated to decreased disability ($p = 0.001$) and depressive symptoms ($p = 0.018$) scores following intervention after adjusting for sex, educational duration, and marital status. There was no significant association ($p = 0.408$) between compliance status and mean decreased in

disability (mean difference: -2.89, 95% CI: -7.37, 1.58) (figure 18). Patients with good compliance to lymphoedema management had depressive symptom scores 1.57 points significantly (p = 0.008) lower than those who poorly complied (95% CI: -2.19, -0.19) after controlling for age and educational duration (figure 19). All pairwise within group differences were significant in both study outcomes (p < 0001). All p-values were Bonferroni-adjusted.

Table 6: Compliance status and its association with study outcome subgroups

N = 161	**Strata**	**Good Compliance n (row %)**	**Poor Compliance n (row %)**		**p-value (Odds Ratio)**
Sex	Female	129 (88.4)	17 (11.6)		**0.002 (5.2)**
	Male	9 (60.0)	6 (40.0)		
Educational duration	<10 years	75 (82.4)	16 (17.6)		0.200 (0.54)
	≥ 10 years	63 (90.0)	7 (10.0)		
Highest stage	2	63 (94.0)	4 (6.0)		**0.011 (3.95)**
	3	75 (79.8)	19 (20.2)		
Life Partner	Yes	68 (87.2)	10 (12.8)		0.627 (1.25)
	No	70 (84.3)	13 (15.7)		
Age group (years)	18-44	79 (89.8)	9 (10.2)		0.132 (1.98)
	≥ 45	62 (81.6)	14 (18.4)		
Outcome variables (N=161)	**Highest Stage**	**Outcome status**	**Good compliance n (row %)**	**Poor compliance n (row %)**	**p-value**
Functional improvement	2	Good	47(94.0)	3(6.0)	0.742
		Poor	16(94.1)	1(5.9)	
	3	Good	53(77.9)	15(22.1)	0.428
		Poor	22(84.6)	4(15.4)	
Depressive Symptoms	2	Improved	48(96.0)	2(4.0)	0.258
		Unimproved	15(88.2)	2(11.8)	
	3	Improved	44(75.9)	14(24.1)	0.149
		Unimproved	31(83.8)	6(16.2)	

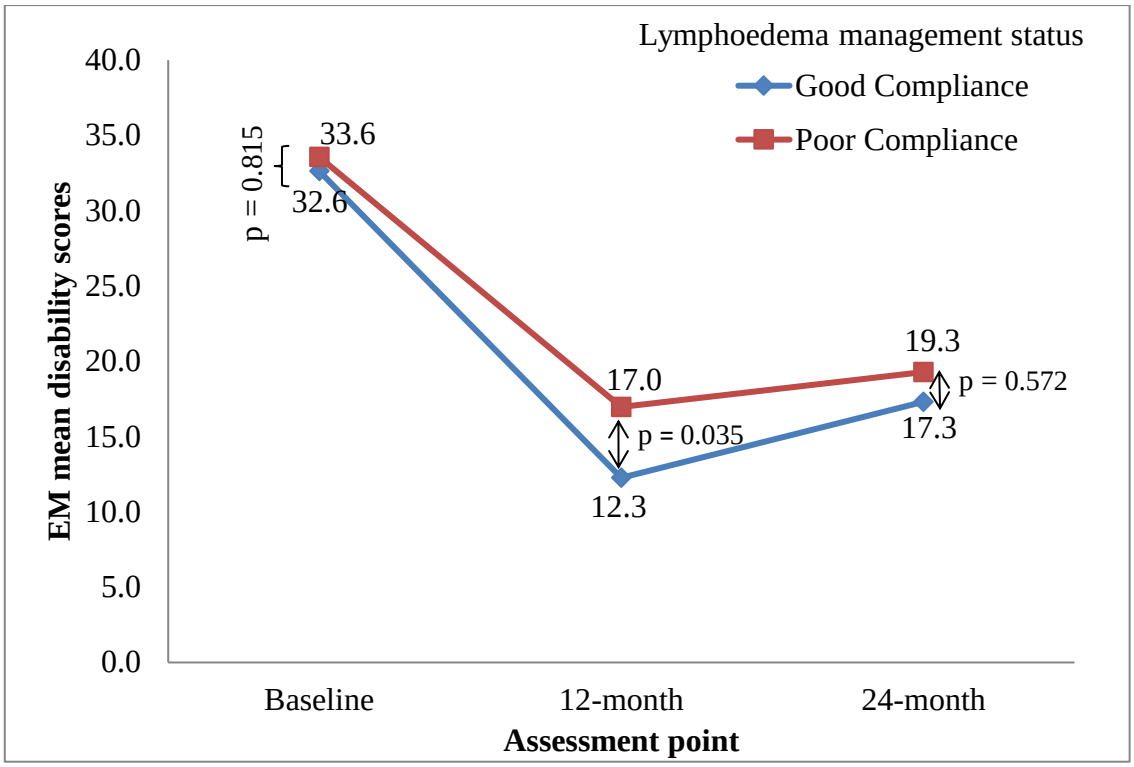


Figure 18: Estimated marginal mean of perceived disability by compliance status

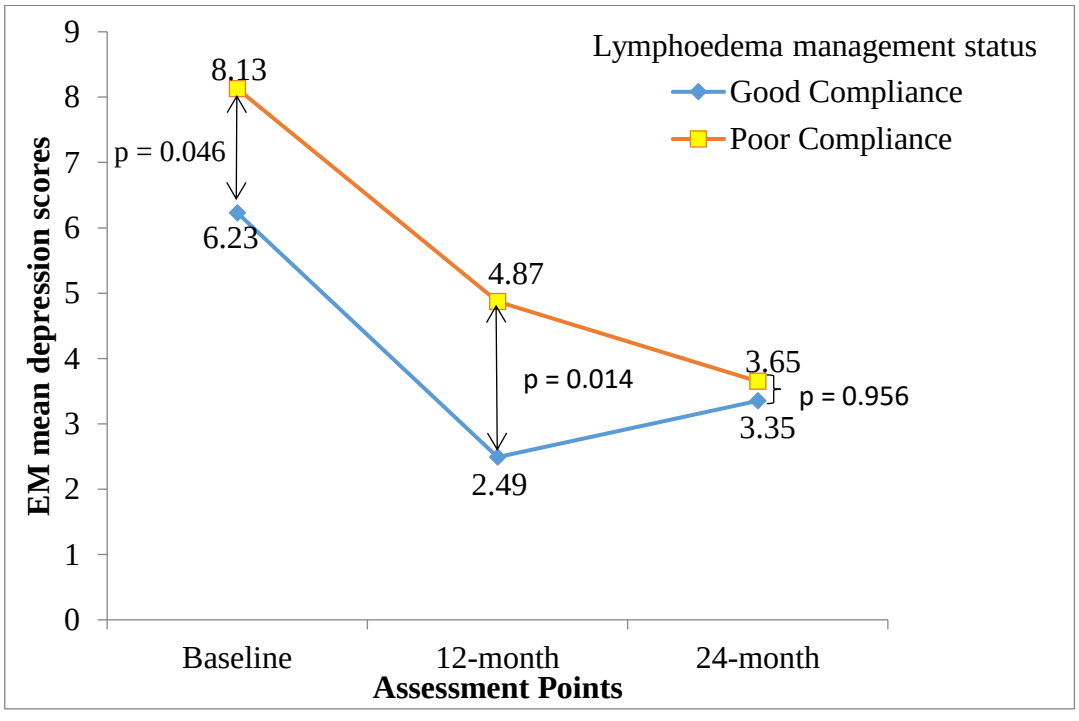


Figure 19: Estimated marginal mean of depressive symptoms by compliance status

4.5 Association between compliance status and podoconiosis related QoL improvement status at 24-month

Base on cut off points used in PHQ-9 and WHODAS 2.0, absence of ADLA, and a decrease day(s) of work lost characterising good QoL improvement; 57% of participants who reported to have highly adhere (good compliance) to lymphoedema management back at home had clinically significant improvements while 5% who partially adhere (poor compliance) to management had unimproved QoL at 24-month. There was a 10.2% increase of having an improved QoL among participants who had a good compliance to lymphoedema management over those who poorly adhered (OR = 1.102, 95% C.I: 0.436, 2.785) (figure 20).

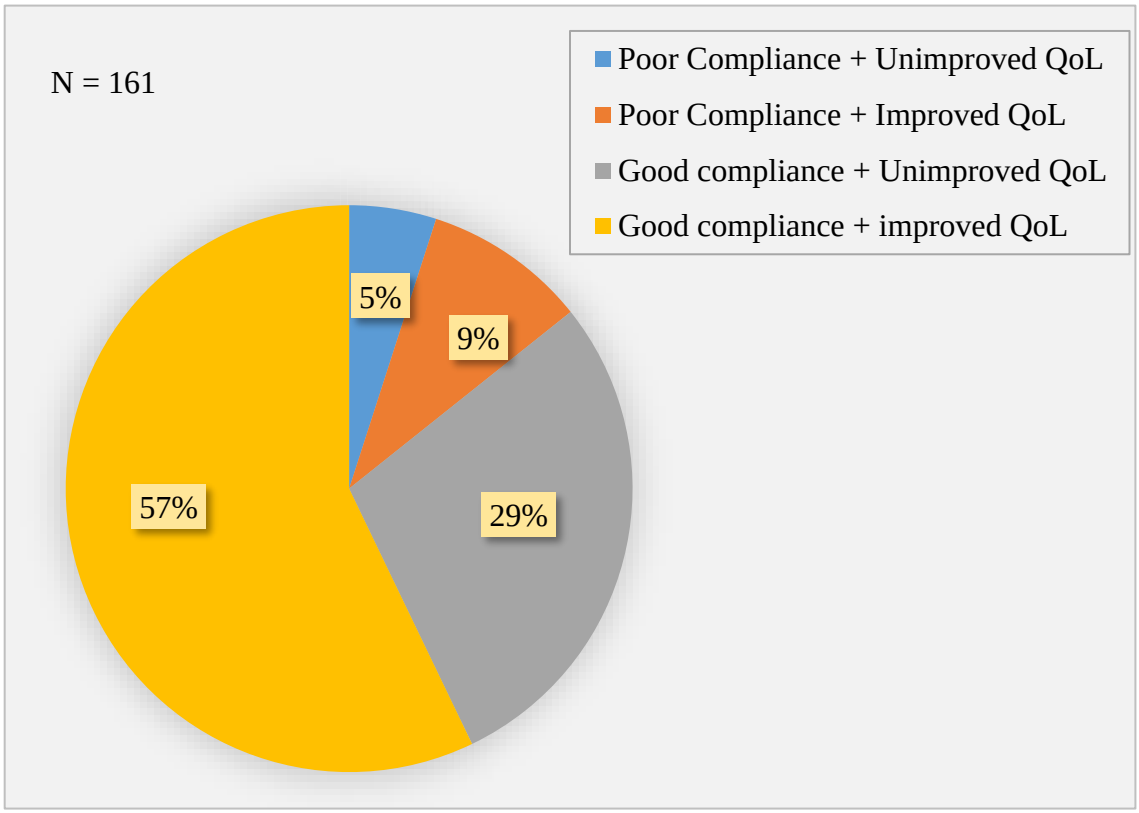


Figure 20: Proportion of participants with clinically significant improvement in QoL at 24-month

CHAPTER FIVE

DISCUSSION, CONCLUSION, RECOMMENDATIONS AND PERSPECTIVES

5.1 Discussion

Our understanding of the gravity of this non-filarial elephantiasis is still incomplete although several studies have stated significant adverse impacts of podoconiosis on physical and mental health not leaving out quality of life related to it. Podoconiosis patients frequently report depression, embarrassments, and social isolation even at early stages of the disease (Bartlett *et al*., 2016; Semrau *et al*., 2019; Semrau *et al*., 2020). The stigma of lymphoedema creates barriers both to health seeking and adherence to recommended treatment further leading to social disconnectedness, which in turn contributes to depression (Person *et al*., 2009).

Moreover, increased frequency of acute attacks (inflammatory episodes) has been showed to have had negative impact on socio-economic status through decreasing ability to work and leading to disability. As a result of the burden of the disease on its patients without any clear or consensual intervention to help ameliorate their condition and because there are limited studies which evaluated the effect of podoconiosis lymphoedema management on patient's disability and depressive symptoms, it was of great importance to carry out this research. Significant association has been proven between hygiene-based intervention reduction in ADLA and morbidity (disability) in NTDs affecting the skin (Eze *et al*., 2020).

The lasting effect of morbidity management on socio-demographic strata showed a general drop in the odds of functional limitation and depressive symptoms at 12 and 24 months follow-up when compared to baseline. The odds of functional limitations amongst self-employed subgroup decreased from baseline (1.63) to midline (0.45) and endpoint

(0.44) following intervention. At baseline there was a 63% higher odd of functional limitations while at endpoint there was a 44% lower odds of functional limitations due to morbidity management. This implied there was functional improvements amongst self-employed (being the subgroup with about 4 times as much participants as there were in "other occupation" subgroup) as their WHODAS 2.0 scores decrease significantly at 12 and 24-month. The strength of the association gravitates towards 0 (no relationship) as the proportion of participants with functional limitation at baseline turn to have no disability following morbidity management. These findings were consistent to those demonstrated by Chiang and colleagues who used the WHODAS 2.0 to assess functional impairment in people with depression who were either employed or not and found out that there were higher odds of having functional improvement (as their disability scores decreases with time) in participants who stayed employed after a period of 3 years (Chiang *et al*., 2021). However, results on living as in couple, higher educational duration, and being employed as a homemaker or student were significantly associated to lower disability scores over time in a study carried out in Orissa (Budge *et al*., 2013) on filarial elephantiasis patients. This was contradictory to our study.

Morbidity management generally decreased podoconiosis related depressive symptoms scores with time and this affected the association between depression and demographic variables. Employment, age and educational duration subgroups were significantly associated to depression at baseline. The strength of the relationship however grew weaker following intervention. The odds of having depressive symptoms among farmers/self-employed compared to other professions dropped from 5.01 at baseline to 2.63 and 1.32 following morbidity management. This could be because participants religiously practiced lymphoedema hygiene management back at home as they were taught at the Centre during each visit. This was in line with studies carried out using the

Taiwan Databank of Persons Disability (TDPD) where basic treatment for major depressive disorder was reported to have had partial functional improvement in either groups and the adjusted odds ratios of functional improvement in the employment group indicated an increased likelihood of recovery from disabilities (Chiang *et al*., 2021).

This study found that the disability severity status had remarkably reduced from baseline to 24 months follow up across all domains. About 28.5% of the participants who previously had at least some disability level (functional limitations) reported to have had none at 12-month and 16.7% at 24-month following morbidity management intervention. The proportion of participants with moderate-severe disability decreases from 61.4% at baseline to 21.1% and 28.6% at midline and endpoint respectively. This finding was in line with a study tackling the effectiveness of self-care intervention for integrated morbidity management of skin NTDs in Anambra state, Nigeria and the slight proportion discrepancies were due to different cut-off points used in the study (Eze *et al*., 2021). The significant decrease ($p < 0.001$) in the medians of the six domains of WHODAS 2.0 scores (first 3 domains measured activity limitations while the last 3, participation restriction) inferred functional improvement following intervention. These findings were consistent with results on the impact of community-based lymphoedema management on perceived disability among patients with lymphatic filariasis in Orissa State where less disability was experienced in almost every domain sustained in two years. Unlike our study, there was no significant decrease in the mobility and self-care domains among patients with lymphatic filariasis comparing baseline to endpoint. The overall median perceived disability score in our study decreased significantly from 31.3 at baseline to 8.4 at midline and 14.6 at 24 months follow-up; this finding was similar to studies carried out by Budge and colleagues (Budge *et al*., 2013). Furthermore, these results also aligned with that of a recent study carried out in Matara, Sri Lanka where dermatology life quality index

(DLQI) (having slight modifications with WHODAS 2.0 for simplicity) was used to measure QoL in MMDP program for lymphatic filariasis. The modified DLQI mean score reduced significantly from 4.1 to 1.9 among 27 patients after one year of lymphoedema care (Yahathugoda *et al*., 2018).

Lymphoedema management has been known to be associated with decrease acute attack frequency and days in which the participant was totally unable to work or execute other activities (Budge *et al*., 2013; Enbiale *et al*., 2021). This reduction in disability can have significant economic impact on both patients and their communities. Our study demonstrated that there was a significant drop in the mean days of work totally lost from 2.6 at baseline to 1.3 at endpoint. If extrapolated to the estimated 41556 podoconiosis cases in Cameroon, this translates into approximately 3553 person-years of productive time gained over the course of the 24 months period. This may greatly increase the agricultural output in the Region since most of the patients are farmers (especially in high prevalence areas like Bafut, Batibo and Njikwa) and help boost the country's economy. Participants gained an average of 1.3 workdays per month as a result of decreased perceived disability. These results were similar with those reported by Budge and colleagues where an average of 2.4 workdays per month was gained by LF patients following a 24 months morbidity management program. If extrapolated to all 17036 lymphatic filariasis patients, an estimate of 2688 person-years of productive time would be gained over 24 months study period (Budge *et al*., 2013).

Depression has been demonstrated to be strongly and positively associated to disability. A study on the impact of mental health care on clinical and functioning outcomes of people with depression and alcohol use disorder in Nepal demonstrated that there was no significant difference ($p = 0.073$) in the mean adjusted changes in PHQ-9 between baseline and midline or endline (Jordans *et al*., 2020). Jordans and colleagues also stated

that a cut-off of 10 implied an optimal score to indicated high risk of depression. By this criteria, 20% (5% severe and 15% moderate depression) of the participants at baseline were at high risk of depression and this proportion dropped to 6% at midline and 5% at 24-month hence improving the quality of life of more podoconiosis patients. These findings were similar to ours where a significant difference ($p < 0.0001$) was shown with a baseline median (25th and 75th percentile) of 6.0 (3, 9) which decreased to 2.0 (0, 4) at 12-month and 3.0 (1, 5) at endline following morbidity management. The proportion of participants with no depressive symptoms stepped up by approximately 4 folds at 12-month and 3 folds at 24 months.

Recent studies on QoL have demonstrated that occurrence of ADLA episodes, depressive symptoms, functional limitations, and days of work lost are strongly associated with poor quality of life related to podoconiosis. The QoL improvement status was measured based on these factors as they greatly contribute to emotional well-being and economic productivity (Stocks *et al*., 2015; Yahathugoda *et al*., 2018). Budge and colleagues reported that the only individual component of lymphoedema management which was significantly related with reduced disability levels was wearing shoes with a 2.8 mean score decrease (95% C.I: -4.6, -1.1). However, other components of lymphoedema management adherence showed no significant association with decreased scores (Budge *et al*., 2013). This was in line with our study where compliance strata had no significant relationship with disability (adjusted mean difference = -2.89 at 95% C.I: -7.37, 1.58). There was no need in stratifying participants into shoes wearing or not as all participants in our study wore shoes or worst-case scenario sandals.

Interestingly, patients with good compliance to lymphoedema management had mean depressive symptoms scores 1.57 points significantly lower ($p = 0.008$) than those who poorly complied (95% CI: -2.19, -0.19) (figure 19)). Menza and colleagues reiterated that

depression had been associated with poorer treatment compliance and greater caregiving distress amongst Parkinson disease sufferers (Menza *et al.,* 2009).

There was however a significant decrease in both disability ($p = 0.035$) and depressive ($p = 0.014$) symptoms EM mean scores with good compliance group having lower estimated marginal mean scores at 12-month follow-up. A possible explanation for this result may be related to the intensity of the intervention, the regularity and seriousness of the participants to adhere to treatment (management) during the first half of the program whereby they frequently visited the centre at 3 time points (2 months, 4 months and 6 months) and were supported with items to help them practice lymphoedema management back at home.

Surprisingly, the mean scores at 24-month were higher (though not statistically significant) compared to those at 12-month assessment point. This increase can be explained by the fact that during the 3 last visits (12 months, 18months and 24 months follow-up), participants were asked to come at intervals of 6 months (rather than the normal 2 months interval they started with) where only 60% of participants respected their visit window without discontinuing. The Covid-19 pandemic and measures put in place (by the Bamenda Clinical Trial Centre in consonant with that of the Cameroon Ministry of Public Health) to prevent or reduce the chances of participants and staff from being infected by the novel corona virus, coupled with the already existing socio-political crises could be amongst the top reasons why there was the slight increase in both disability and depressive symptoms mean score from 12 to 24-month assessment point. More so, it was only during this period that participants complained of their Vaseline getting finished and difficulties in getting or purchasing an original ointment from the market or local cosmetic shops. Some adopted the use of palm oil after washing their legs with soap. Summarily, negligence on the part of the patients due the fact that they saw drastic

improvements and neglected foot hygiene management, decreased frequency of visit due to Covid-19 prevention strategies on the part of the Morbidity Management Center, and other difficulties to travel such as lockdowns could be possible reasons for the slight score increase in mean scores following management at 24-month.

In this study, 57% of the participants had clinically improved QoL (based on significant decreased scores from baseline on factors proven to be strong predictors of QoL) at 24-month among patients who reported to have “goodly" adhere to lymphoedema management while 29% who reported to have fully adhere to the management had a clinically unimproved QoL. The odds of poor podoconiosis related quality of life among participants with higher educational years who reported to have had a good compliance to lymphoedema management were 1.21 times higher compared to those who poorly complied. Educational duration could be a confounding factor to this 29% (who had a good compliance but unimproved QoL). Nine percent of podoconiosis participants who poorly complied to management had an improved quality of life.

This could primarily be because patients accepted podoconiosis as a disease and not a mystical punishment. Secondly, they felt cared and grateful for the intervention and its benefits on their health (which by definition is a state of complete physical and social wellbeing and not just the absent of a disease or infirmity) as a whole. This greatly played a role in increasing patient self-worth, mental and psychological health, hence addressing the issue of stigmatisation associated to the disease (Semrau *et al*., 2019; Deribe *et al*., 2013).

5.2 Conclusion

The following conclusions can be drawn from this study;

1. Morbidity management significantly decreases disability at 12 and 24 months from baseline.
2. The intervention (morbidity management) also decreases depressive symptoms 12 and 24 months following intervention hence improving the quality of life of podoconiosis participants in the North West Region.
3. Good compliance to lymphoedema management further decreases disability and depression severity following measure sequence, likewise the number of days participants were totally unable to work or school.

5.5 Recommendations

1. More morbidity management prevention centres should be built in Regions with high podoconiosis prevalence. More attention should be given to patients with higher complicated stages who could not properly take care of their legs (poor compliance to lymphoedema management). They should be rehabilitated and properly cater for till they are fit to continue the regimen independently.
2. The Ministry of Public Health should integrate podoconiosis treatment package and train health workers on how to collect data using quality of life, disability and depressive symptoms assessment instruments related to podoconiosis to detect changes (improvements and deteriorations) due to treatments.
3. The population should be sensitised about the disease. This will help reduce depression and stigma hence might improve on patients' interactive and cognitive function particularly.
4. These results reported emphasised the need for a national lymphoedema morbidity management and prevention program to improve peoples' quality of lives suffering from lymphoedema due to podoconiosis.

5.6 Perspectives

Avenues for further research include;

- To evaluate the impact of a two follow-up morbidity management schemes (daily and monthly) on the disability and QoL of podoconiosis patients in the western highlands of Cameroon using context fitting disability and QoL questionnaires specific to podoconiosis.
- To perform a systematic review and meta-analysis on the impact of different lymphoedema morbidity management techniques on disability, depression, mental distress, and QoL in patients suffering from elephantiasis of any origin globally.

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APPENDICES

APPENDIX 1: RESEARCH PARTICIPANT INFORMATION/CONSENT

RESEARCH TOPIC: Effects of Morbidity management on disability and depressive symptoms of podoconiosis patients, 12 and 24 months following intervention in the North West Region of Cameroon. April 2021 to March 2022

Investigator: NDEUGUE NOUYOU MICHEL

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Lecturer, department of Biomedical Sciences, Faculty of Health Science University of Buea

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PURPOSE OF STUDY: The purpose of this study is to help bridge the gap that exists in the treatment of podoconiosis with an expected outcome of assessing any improvement in the quality of life reflected by a reduction in disability (scores) and depressive symptom of the participants in the North West Region of Cameroon.

PROCEDURE: Questionnaires administration before intervention (at baseline), 12 and 24 months following intervention using WHODAS 2.0 and PHQ 9 instruments.

BENEFIT: Participants will have an effective intervention which will help clinicians and health workers to accurately treat them. The findings will be shared to policy makers for informed decisions such as creating morbidity management centres in various regions in the country.

RISKS: Any advert effect was freely taken care of at the clinical trial center.

CONFIDENTIALITY: Personal and sensitive data concerning participants are securely and strictly kept.

COMPENSATION: Participants will benefit from free treatment of any adverse event from the drug administered and at the end of the trial; they will be place under effective treatment. Soap and Vaseline oil are given to participants during each visit so that they can continue lymphoedema management as taught at the center.

CONSENT: I have received a copy of this information, have read or had it read to me, and understood its contents. I therefore accept to take part in this study knowing that participation is voluntary and that I reserve the right to withdraw at any time without bearing any prejudice.

Participant’s signature: _____ Investigator’s signature: _____

Date: ___/___/_____

TAKeOFF – PodoLEDoxy

Title: Doxycycline for treatment on non-filarial lymphoedema due to podoconiosis (PodoLEDoxy) - a randomised double blinded placebo-controlled trial

Principal Investigator: Prof. Samuel Wanji; Department of Microbiology and Parasitology, University of Buea, P.O. Box 63, Buea, Cameroon, **swanji@yahoo.fr**

Additional consent form for adults participating in the TAKeOFF-PodoLEDoxy study for sample storage, reutilisation and shipment

Name of the participant (in block letters): _____

Date of birth (year of birth, if exact date is unknown): |__|__| / |__|__| / |__|__|__|__|
(dd / mm / yyyy)

Indiv. No.: |__|__| - |__|__|__| - |__|__|__|
(country) - (village code) - (consecutive patient no)

I hereby certify that the contents of the Patient Information Sheet and the Informed Consent Form have been read by me/ interpreted and explained to me in detail in a language I understand (Pidgin, English, French), (*underline applicable*).

By:_____
(Name of investigator in block letters)

The information given to me has permitted me to make a fully informed and free decision about the storage, reutilisation and shipment of aliquot of the blood, urine, and any tissue samples. If any of the skin swab samples I have provided for this research project is unused or leftover.

☐ I give permission for my blood sample to be stored.

☐ I give permission for aliquots of my blood sample to be shipped to the German Universities of Bonn or Munich or to the institutions in Tanzania and Ghana

☐ I give my permission for aliquots of my blood sample to be stored and used in future research which has received proper ethical approval from the responsible ethics committee

or

☐ I give permission for aliquots of my blood sample to be stored and used I future research except for research about _____(name type of research)

Urine

☐ I give permission for my urine sample to be stored.

☐ I give permission for my urine sample to be shipped to the German Universities of Bonn or Munich or to the institutions in Tanzania and Ghana

☐ I give my permission for my urine sample to be stored and used in future research which has received proper ethical approval from the responsible ethics committee

Or

☐ I give permission for urine sample to be stored and used in future research except for research about _____(name type of research)

I am aware that I can withdraw my consent at any time and for any reason without penalty or loss of benefits. By signing this consent form, I do not waive any legal rights, and the investigator(s) or sponsor are not relieved of any liability they may have.

I thereby append my signature/ mark (right thumbprint) to this Informed Consent Form, as evidence of my agreement to storage, re-utilisation and shipment of my samples.

Date: |__|__| / |__|__| / |__|__|__|__|
(dd / mm / yyyy)

If needed, thumbprint of participant:

_____
(Participant's signature)

_____
(Participant's name in block letters)

WITNESS (independent from research team)

I hereby certify that I was present when the contents of the Patient Information Sheet and the Informed Consent Form were read/interpreted and explained in the language (Pidgin, English, French), (*underline applicable*) to

_____
(Name of participant in block letters)

He/she seems to have fully understood the contents of the Patient Information Sheet and the Informed Consent Form before appending his/her signature or making his/her mark (right thumb print) to this Informed Consent Form. As the legal representative I hereby agree with his/her agreement to storage, re-utilisation and shipment of his/ her samples.

Date: |__|__| / |__|__| / |__|__|__|__|
(dd / mm / yyyy)

If needed, thumbprint of parent:

_____
(Signature of the witness)

_____
(Name of the witness in block letters)

Informant (Investigator)

I hereby certify that the contents of the Patient Information Sheet and the Information Consent Form were interpreted and explained by me in a language he/she understands ((Pidgin, English, French) (underline applicable)).

_____
(Name of the participant in block letters)

He/she seems to have fully understood the contents of the Informed Consent Form before appending his/her signature or making his/her mark (right thumb print) to this Informed Concern Form in my presence as evidence of his/her agreement to storage, re-utilisation and shipment of samples.

Date: |__|__| / |__|__| / |__|__|__|__|
(dd / mm / yyyy)

_____
(Signature of the investigator)

_____
(Name of the investigator in block letters)

APPENDIX 2: PARTICIPANT QUESTIONNAIRES

2. 1 World Health Disability Assessment Schedule Version II (WHODAS 2.0)

This questionnaire contains the interviewer-administered, 12-item version of WHODAS 2.0. Instructions to the interviewer are written in bold and italics – do not read these aloud Text for the respondent to hear is written in standard print in blue. Read this text aloud Facet sheet

Complete items F1–F5 before starting each interview				
F1	Respondent identity number			
F2	Interviewer identity number			
F3	Assessment time point (1, 2, etc.)			
F4	Interview date	_____ Day	_____ month	_____ Year
F5	Living situation at time of interview (circle only one)	Independent in community		1
		Assisted living		2
		Hospitalised		3

Please continue to next page...

Demographic and background information

This interview has been developed by the World Health Organisation (WHO) to better understand the difficulties people may have due to their health conditions. The information that you provide in this interview is confidential and will be used only for research. The interview will take 5–10 minutes to complete.

For respondents from the general population (not the clinical population) say:

Even if you are healthy and have no difficulties, I need to ask all of the questions so that the survey is complete.

I will start with some background questions

A1	***Record sex as observed***	Female	1
		Male	2
A2	**How old are you now?**	_____ years	
A3	**How many years in all did you spend studying in school, college or university?**	_____ years	
A4	**What is your current marital status?** ***(Select the single best option)***	Never married	1
		Currently married	2
		Separated	3
		Divorced	4
		Widowed	5
		Cohabiting	6
A5	Which describes your main work status best? ***(Select the single best option)***	Paid work	1
		Self-employed, such as own your business or farming	2
		Non-paid work, such as volunteer or charity	3
		Student	4
		Keeping house/ homemaker	5
		Retired	6
		Unemployed (health reasons)	7
		Unemployed (other reasons)	8
		Other (specify)_____ _____	9

Please continue to next page…

Core questions: The interview is about difficulties people have because of health conditions. When answering, I would like you to think back over the past 30 days. I would also like you to answer these questions thinking about how much difficulty you have had, on average, over the past 30 days, while doing the activity as you usually do it						
In the past 30 days, how much difficulty did you have in:		None	Mild	Moderate	Severe	Extreme or cannot do
S1	Standing for long periods such as 30 minutes?	1	2	3	4	5
S2	Taking care of your household responsibilities?	1	2	3	4	5
S3	Learning a new task, for example, learning how to get to a new place?	1	2	3	4	5
S4	How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	1	2	3	4	5
S5	How much have you been emotionally affected by your health problems?	1	2	3	4	5
In the past 30 days, how much difficulty did you have in:		None	Mild	Moderate	Severe	Extreme or cannot do
S6	Concentrating on doing something for ten minutes?	1	2	3	4	5
S7	Walking a long distance such as a kilometre [or equivalent]?	1	2	3	4	5
S8	Washing your whole body?	1	2	3	4	5
S9	Getting dressed?	1	2	3	4	5
S10	Dealing with people you do not know?	1	2	3	4	5
S11	Maintaining a friendship?	1	2	3	4	5
S12	Your day-to-day work/school?	1	2	3	4	5
H1	Overall, in the past 30 days, how many days were these difficulties present?			*Record number of days ____*		
H2	**In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?**			***Record number of days ____***		
H3	In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?			*Record number of days ____*		
This concludes our interview. Thank you for participating.						

2. 2: Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✓" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
FOR OFFICE CODING = Total Score: _____	_____	_____	_____	_____

Summary of QoL related to depression due to podoconiosis

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?			
Not difficult at all ☐	Somewhat Difficult ☐	Very difficult ☐	Extremely difficult ☐

2. 3: Hygiene Assessment Form

HYGIENE ASSESSMENT FORM A

Interviewer/Examiner: _____

Date: |__|__| / |__|__| / |__|__|__|__| Time**:** |__|__|:|__|__| ☐ AM ☐ PM
(dd/mm/yyyy) (h:min)

QUESTIONS ADDRESSED TO THE PATIENTS

1. When did you last wash the limb(s)?

☐ Today ☐ Yesterday ☐ More than 2 days ago

2. How many times a day do you generally wash your affected limb(s)?

☐ Less than once a day ☐ Once ☐ Twice ☐ Three or more times

3. Where does the washing take place?

☐ At home ☐ At water source (e.g. community tap, well)
☐ Other place (Describe:_____)

4. Where do you get the water for washing?

☐ Carried to me ☐ I go to the water source

5. Do you use soap while you are washing? ☐ Yes ☐ No

6. Does anybody help you to wash your affected limb(s)? ☐ Yes ☐ No

7. Do you use any other things other than soap on the skin of your affected limb?

☐ Yes ☐ No If yes, what do you use?
_____

8. What do you do with your affected limb or limbs when you are sitting down?

☐ Keep level (of hip) ☐ Hang down ☐ Elevate

9. What do you do with your affected limb or limbs when you are sleeping?

☐ Keep level ☐ Hang down ☐ Elevate

INDEPENDENT OBSERVATIONS BY INTERVIEWER

These are assessments made by an external observer without any major input from the patient himself/herself. It will be important to have carefully compiled baseline assessment, optimally with photographs of the major sites on each leg (both affected and unaffected if it is a unilateral condition). Images of the toes, inter-digital areas, heels, ankles and mid-calf areas are suggested as basic photos.

A. Skin and nail status

Cleanliness of the skin (both legs):

☐ Clean ☐ Partially clean ☐ Obviously dirty

Presence of dirt on the toes-nail bed:

☐ Clean ☐ Partially clean ☐ Obviously dirty

Status of the toe nails:
☐ Cared for ☐ Unkempt ☐ Absent
Status of skin between the toes:
☐ Normal ☐ Poor state ☐ Open cracks present
Presence of skin breaks/cracks on heels:
☐ Normal ☐ Poor state ☐ Open cracks present
Cleanliness of skin folds:
☐ Clean ☐ Partially clean ☐ Obviously dirty ☐ Not applicable
Presence of open wounds on limb:
☐None ☐Uninfected wound(s) present ☐Compromised wound(s) present
Comments (skin and nail status, only to be filled if really necessary):

B. Facilities (UA= unable to assess)
Has soap present in washing area (home, etc.): ☐ Yes ☐ No ☐ UA
Has obvious source of water for washing: ☐ Yes ☐ No ☐ UA
Basin and towel for washing evident: ☐ Yes ☐ No ☐ UA
C. Overall assessment (UA= unable to assess)
Limb clearly kept washed and clean: ☐ Yes ☐ No ☐ UA
Comments (facilities and overall assessment, only to be filled if really necessary):

APPENDIX 3: ETHICAL CLEARANCE

COMITE NATIONAL D'ETHIQUE DE LA RECHERCHE POUR LA SANTE HUMAINE

Arrêté N° 0977/A/MINSANTE/SESP/SG/DROS/ du 18 avril 2012 portant création, organisation et fonctionnement des comités d'éthique de la recherche pour la santé humaine au sein des structures relevant du Ministère en charge de la santé publique

N° 2020/12/1330/CE/CNERSH/SP Yaoundé, le 03 décembre 2020

Cnethique_minsante@yahoo.fr

RENOUVELLEMENT DE LA CLAIRANCE ETHIQUE

Le Comité National d'Ethique de la Recherche pour la Santé Humaine (CNERSH), en sa session ordinaire du 03 décembre 2020, a examiné le projet de recherche intitulé : **«Doxycycline for treatment of non filarial lymphedema due to podoconiosis (PodoLE) – a randomized double blind placebo-controlled trial»** soumis par le **Professeur Samuel WANJI,** Investigateur Principal, Université de Buéa.

Le projet est d'un grand intérêt scientifique et social. Cette étude a déjà bénéficié d'une clairance éthique (réf. N°2018/05/1002/CE/CNERSH/SP) du 03 mai 2018 et d'un renouvellement de la clairance éthique (réf. N°2019/02/1145/CE/CNERSH/SP) du 21 février 2019. Le Comité a pris acte de l'état d'avancement du projet. La dernière version approuvée n'a subi aucune modification ayant un impact éthique. La procédure de l'étude est bien documentée et claire. Pour toutes ces raisons, le Comité National d'Ethique approuve pour une durée d'un an la mise en œuvre de la présente version du protocole.

Les Investigateurs sont responsables du respect scrupuleux du protocole approuvé et ne devraient y apporter aucun amendement aussi mineur soit-il, sans avis favorable du CNERSH. Les investigateurs sont appelés à collaborer pour toute descente du CNERSH pour le suivi de la mise en œuvre du protocole approuvé. Le rapport final du projet devra être soumis au CNERSH et aux autorités sanitaires du Cameroun.

La présente clairance peut être retirée en cas de non respect de la réglementation en vigueur et des recommandations susmentionnées.

En foi de quoi, la présente clairance éthique est délivrée pour servir et valoir ce que de droit.

Ampliations

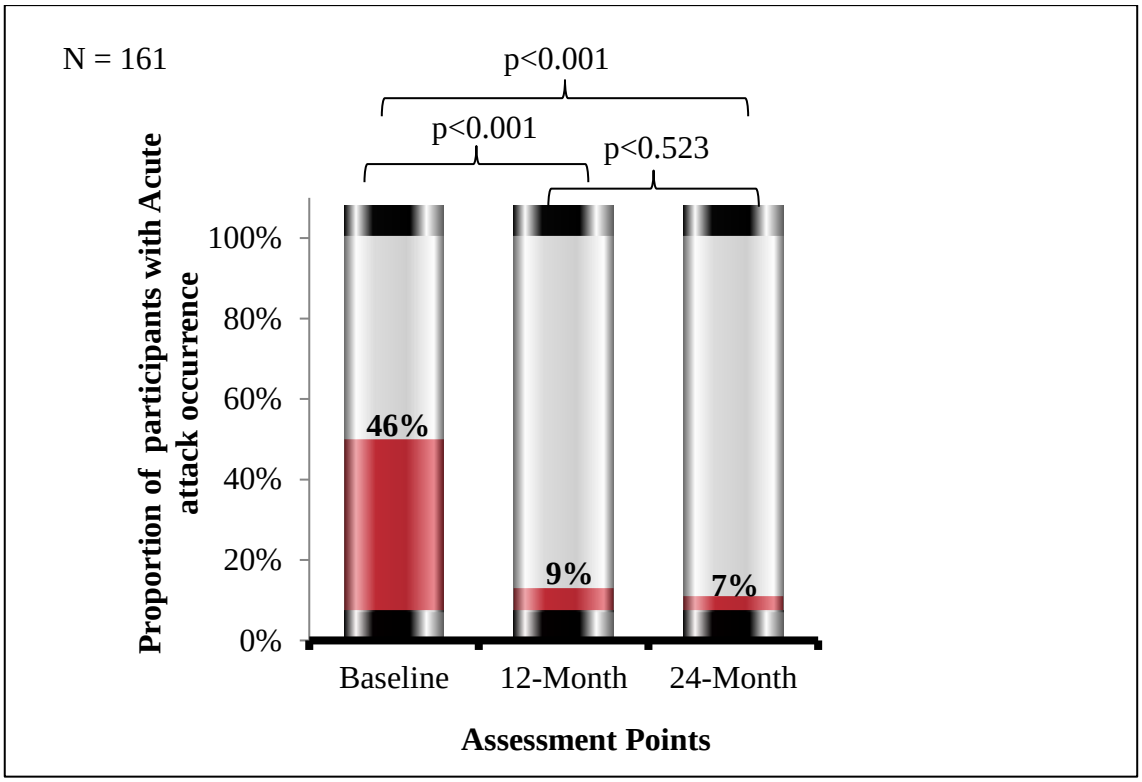
- MINSANTE

Le Président

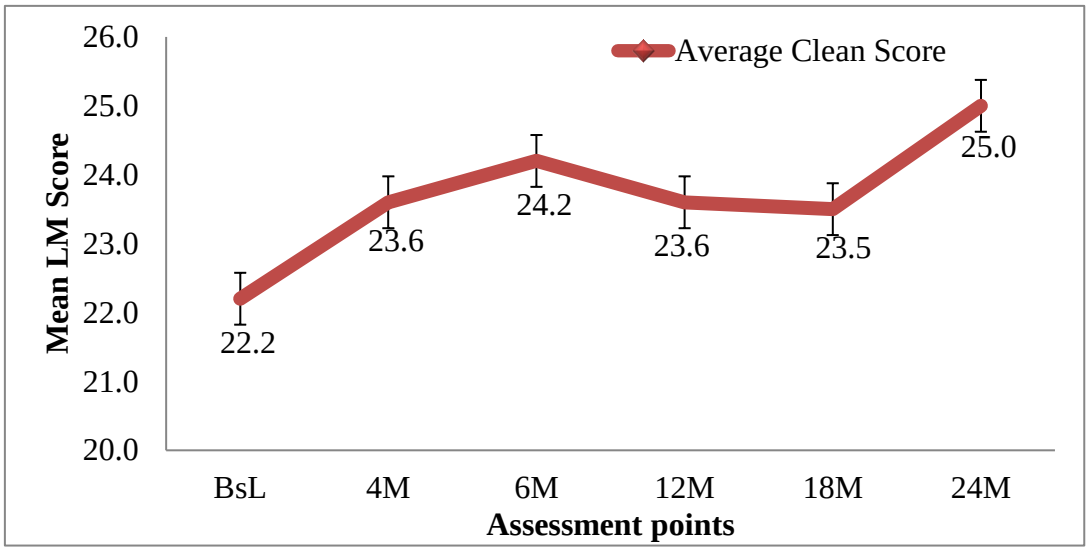
Pr Lazare KAPTUE

N.B : cette clairance éthique ne vous dispense pas de l'autorisation administrative de recherche (AAR), exigée pour mener cette étude sur le territoire camerounais. Cette dernière vous sera délivrée par le Ministère de la Santé Publique.

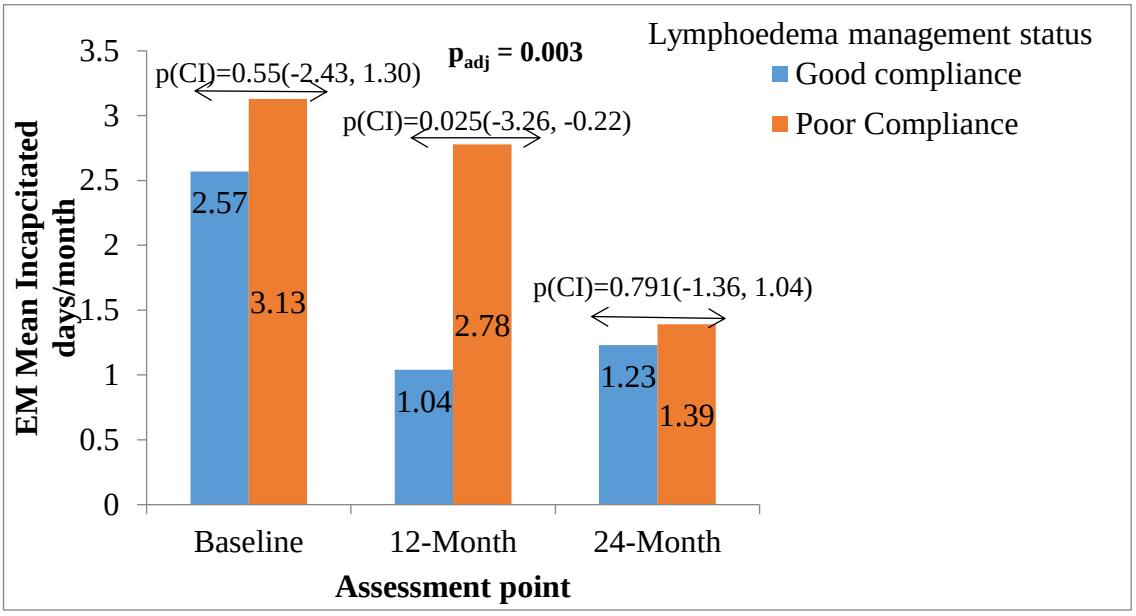
APPENDIX 4: SUPPLIMENTARY RESULTS



ADLA attack proportions in participants following at baseline and following morbidity management (McNemar Test)



Lymphoedema management and foot care average score following measure sequence



Supplementary results on days totally unable to work/month per Lymphoedema management compliance status (Repeated measures - generalized linear model)

p_{adj} = 0.003 was the Bonferroni adjusted p-value for pairwise comparisons amongst the estimated marginal means

Table showing days with difficulty and suicide ideation in podoconiosis patients

	Baseline	Midline	Endpoint
Proportion of participants with difficult days per month (H1) N (%)			
No day	4(2.5)	37(23.0)	25(15.5)
1 -6 days	40(24.8)	66(41.0)	51(31.7)
More than 7 days	117(72.7)	58(36.0)	85(52.8)
Average days/month (SD)	13.2(9.1)	6.7(8.2)	9.6(9.2)
Proportion of participant with suicide ideation	36(22.4)	18(11.2)	16(9.9)

Table showing the effect of morbidity management in podoconiosis patients after depressive disorder diagnosis

N = 161	Major depressive Disorder			Other Depressive Disorder			No Depressive Disorder		
Assessment points	Compliance status								
	Good	Poor	**Total**	Good	Poor	Total	Good	Poor	Total
Baseline	11	3	**14**	37	6	**43**	90	14	**104**
12-Month	1	2	**3**	18	2	**20**	119	19	**138**
24-Month	3	2	**5**	12	3	**15**	123	18	**141**

Table showing comparative analyses between baseline and midline scores of outcome variables in podoconiosis participants who discontinued at 12 months

N=9	Baseline (mean)	12-month (mean)	Mean difference (SD)	95% CI	p-values
Disability	37.3	22.5	14.8 (11.58)	5.9, 23.7	**0.005**
Days totally unable to work/month	4.8	6.2	-1.4 (5.7)	-5.8, 3.0	0.471
Depressive symptoms	7.0	6.4	0.56 (4.6)	-2.95, 4.1	0.724